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TROPICAL DISEASES BULLETIN

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Issued under the Direction of
the Honorary Managing Committee of the

BUREAU OF HYGIENE AND TROPICAL DISEASES

Keppel Street, London, W.C.1

Telephone: Museum 3041

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BUREAU OF HYGIENE AND TROPICAL DISEASES

TROPICAL DISEASES BULLETIN

Vol. 52] 1955 [No. 4

SUMMARY OF RECENT ABSTRACTS *

III. MALARIA †

[Continued from p. 241]

Treatment

The Malaria Sub-Committee of the Colonial Medical Research Committee has issued a detailed set of recommendations for the use of antimalarial drugs, which is printed in full on pp. 861–867 of this *Bulletin*. It deals with actions and usage in treatment and prophylaxis, and gives a full account of dosage, which is related to partially immune as well as to non-immune subjects. This is a most comprehensive document, concise and exact in tone. An informative bulletin has also been issued in Nigeria by Bruce-Chwatt (p. 764), in which the chemoprophylaxis and suppression of malaria are described in detail. The Fifth Report of the Expert Committee on Malaria of WHO (p. 1028) gives a schedule of drugs and doses, and recommends that proguanil and pyrimethamine should be used for prophylaxis only.

Coatney *et al.* (p. 352) have published an extensive monograph which summarizes an enormous amount of work done in screening some 4,000 substances for antimalarial action. The information is tabulated in detail and subdivided according to the chemical constitution of the compounds. The parasite used was *Plasmodium gallinaceum* and the substances were tested for therapeutic and prophylactic activity.

Quinine is still used. Monteny (p. 879) gives it intravenously in chronic malaria in Africans in the Belgian Congo and writes favourably of a dosage of 200 mgm. daily for 4 days, and at a meeting of the Netherlands Society of Tropical Medicine (p. 879) its importance by this route in the treatment of algid malaria was stressed.

A trial in Africa showed that Azacrin, a compound of the acridine series, was an effective schizontocide for *P. falciparum*, being rather more rapid in action than chloroquine and mepacrine; it had no toxic action but tended to cause exacerbation of nausea in children with gastro-enteritis (Ang'awa

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1954, v. 51. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

† For previous articles on malaria in this series see the March and April issues of the *Tropical Diseases Bulletin* each year since 1939.

and Fendall, p. 674). In Malaya Edeson (p. 1224) found it about as effective as mepacrine, though like mepacrine it is not reliable when given as a single dose. It had no apparent action on gametocytes of *P. falciparum*.

Perroni (p. 345) failed to find any adverse effect of proguanil in the treatment of malaria in patients with cardiovascular diseases, for whom he regards it as the drug of choice. Proguanil-resistant strains of *P. falciparum* have been reported in Malaya (Walker and Reid, p. 252) and Assam (Norman, p. 345). Covell (p. 9) states that though proguanil and pyrimethamine are highly effective in the prophylaxis of malaria, they are not suitable for the treatment of acute attacks in non-immune persons. For that purpose chloroquine, amodiaquine and mepacrine are the drugs of choice.

Single-dose treatment with chloroquine has been used successfully by Gaud and Houel (p. 7), Jaswant Singh and Misra (p. 140), Scheel (p. 459) and Wallace (p. 1034). The doses quoted were of the order of 400–600 mgm. of base.

Many studies have been made on the treatment of *P. vivax* malaria with chloroquine given to a total of 1·5 gm. base during 3 days and primaquine (15 mgm. base daily) for 14 days. Coatney, Alving and their colleagues (pp. 460, 675) regard this as the treatment of choice in men returning from Korea, and this opinion is shared by Archambeault (p. 880), but Hansen *et al.* (p. 676) report a few cases of relapse; slightly lower doses were successful in Nicaragua (Thaeler *et al.*, p. 463). In general there has been little sign of toxicity, but in higher doses primaquine may cause haemolysis in Negroes (Coatney *et al.*, p. 460) or even in a man of Caucasian origin (Hansen *et al.*, p. 676). This haemolysis is due to susceptibility of the red cells of the sensitive subject, not to extracorpuscular factors (Dern *et al.*, p. 676). There is no contraindication to the air transport of persons taking primaquine (Chinn and Redmond, p. 1035).

For cure of infections with the Chesson (New Guinea) strain of *P. vivax*, which is characterized by the absence of long-term latency, Cooper *et al.* (p. 462) found that primaquine with quinine was more effective than pamaquin or isopentaquine with quinine. Regimens which were effective against Korean strains, however, were not as successful in infections with the Chesson strain induced by the bites of 10 heavily infected mosquitoes.

Jaswant Singh *et al.* (p. 675) treated *P. vivax* malaria in India with primaquine, pentaquine with quinine, or pamaquin with quinine. The results were good, but in comment Covell suggests that the patients were presumably indigenous people, possessing some tolerance of malaria.

Favourable reports on treatment with amodiaquine have been published (Peter, p. 880; Mein, p. 140; Jame, p. 675). It was used successfully for single-dose treatment (400–600 mgm. base) by Gaud and Houel (p. 7) and by Jaswant Singh *et al.* (p. 140).

Plaquenil is a drug of the 4-aminoquinoline series. Hoekenga (p. 8) used it with some success in Honduras, giving it chiefly by mouth, but in some cases intravenously. It seems to be worthy of further investigation.

At a symposium on pyrimethamine (p. 1222) in India, several speakers made the point that it is not the ideal drug for treatment of the acute attack—especially of *P. falciparum* infection. This opinion is also expressed by Covell and by Woodruff in comments on the papers by Srivastava *et al.* (p. 140) and Giblin (p. 677), who used it in treatment, not always very successfully. Some authors, however, have written favourably on it—Soberón y Parra and Cervantes (p. 531), Treviño *et al.* (p. 530), and Houel (p. 1036) (who gave it as a single dose). The explanation of this

difference of opinion may be that it is more effective in partly immune persons (GIBLIN, p. 677; JASWANT SINGH *et al.*, p. 763), than in non-immune subjects. At the symposium referred to, a claim was made that there was a synergic action with quinine, a point which would bear investigation.

Suppressive treatment

For suppression, a weekly dose of 300 mgm. chloroquine has been found satisfactory in Malaya (WALLACE, p. 1034) and Guatemala (DOBROVOLNY *et al.*, p. 12), and in related dosage in Morocco (HOUEL and VAN GOOR, p. 1035) and in Liberian children (MILLER, p. 1036). In Panama it was as effective as the joint use of hydroxychloroquine and primaquine (CLARK, p. 766).

Amodiaquine has been given each week (300 mgm. base) or each fortnight (600 mgm.) with good results in India (JASWANT SINGH *et al.*, p. 141) and Amazonia (DEANE *et al.*, p. 881). Similar favourable reports are made by HOUEL and VAN GOOR (p. 1035) from Morocco and MILLER (p. 1036) from Liberia.

Pyrimethamine has been widely used in prophylaxis. It has an ample margin of safety (MYATT *et al.*, pp. 11, 531) though very high daily doses, continued for several weeks, have shown toxicity in monkeys (JASWANT SINGH *et al.*, p. 771). It does not appear to be a true causal prophylactic (COATNEY *et al.*, p. 9), but has an adverse effect on gametocytes of *P. vivax* and *P. falciparum* which may be valuable in limiting transmission (SHUTE and MARYON, p. 532). It is highly effective in suppressing the Chesson strain of *P. vivax* in doses of 0·8 to 25 mgm. once each week (COATNEY *et al.*, p. 9). Weekly doses of 25 mgm. gave good results in India (JASWANT SINGH *et al.*, p. 141) though in the Sudan they failed to protect 14 of 15 persons, mostly English, in two households (PHILLIPS, p. 464). Weekly doses of 50 mgm. have been given to children in French West Africa by MASSEGUIN and PALINACCI (p. 533), with success, and, on the other hand, doses as small as 12·5 mgm. every 14 days have been used in African children by BROU (p. 465) though Covell comments that this dosage would favour the production of drug resistance. Monthly doses of 50 mgm. were apparently successful in children in Morocco (HOUEL, p. 1035), but doses up to 100 mgm. were not satisfactory in Tanganyika (CLYDE, p. 678), where there was evidence of development of resistance in *P. falciparum*. In Kenya JONES (p. 677) gave single doses of 100 mgm. at intervals of 6 months followed in some schoolchildren by appropriate monthly doses from the fourth month onwards, but the results were not impressive, and he concluded that pyrimethamine should not be used for mass treatment in hyperendemic areas. Resistant strains of *P. falciparum* were found. In the Belgian Congo CAMPHYN (p. 765) found that 2 doses of 1·92 mgm. per kgm. at an interval of 48 hours protected fully for 45 days and partially for 90, and were more effective than chloroquine or amodiaquine.

HERNANDEZ *et al.* (p. 12) induced resistance in the Chesson strain of *P. vivax* by giving sub-curative doses of pyrimethamine. The resistance persisted through mosquito transmission, and there was cross-resistance to proguanil. Resistance of *P. falciparum* was observed by JELLIFFE (p. 12) in Jamaica and by GROUNDS (p. 679) in Kenya.

Control

General

Although residual insecticides may control malaria there is still a place for attention to water surfaces. KNIPE (p. 142) sums up the basic

principles:—cleaning by removal of obstructions and vegetation, drainage or filling, reduction of surface area of moving water, and making hidden water accessible to control and inspection. Drainage is still maintained as a measure of malaria control in the Naval Base at Singapore, and Southwell-Sander and Thye (p. 17) give a description of the methods used. Colligno and Juillan (p. 1030) record the continuing success of the malaria control methods started in 1927 in relation to a marsh in Algeria.

Insecticides

The Fifth Report of the Expert Committee on Malaria of WHO (p. 1028) takes account of the consistent success which has been recorded in malarial control by modern methods, in all types of difficult circumstances. Recommendations for dosage of insecticides under standard conditions are given.

Residual insecticides may reduce the transmission of malaria by exterminating certain anophelines, by repelling them, or by reducing the survival rate of mosquitoes which have entered houses and fed on gametocyte carriers. Gabaldon (p. 769) makes the point that anthropophilic and endophilic strains are especially affected.

Macdonald and Davidson (p. 770) have made a detailed evaluation of dosage and cycle of application of DDT, BHC and dieldrin in the control of malaria, taking into account not only the killing effect but also the repelling action. In general they regard a 65 per cent. mortality rate of mosquitoes entering a treated shelter as a normal criterion of efficacy. DDT at 2 gm. per square metre every 6 months, *gamma* BHC at 0·2 gm. every 3 months, and dieldrin at 0·6 gm. every 12 months appear to be values of average effectiveness, to be varied according to local conditions.

Rajindar Pal *et al.* (p. 121) have investigated the relationship between the physical forms of DDT and their biological effectiveness as larvicides.

Delicate experiments with larvae of *Anopheles gambiae* indicate that DDT, in addition to acting as a stomach poison, can affect the larvae by way of the spiracular apparatus (Christie, p. 1225).

In one part of Italy, where residual spray campaigns were carried out for several years, they have now been discontinued for some years, without reappearance of the vectors or of malaria, and Raffaele and Coluzzi (p. 533) think that if vigilance is exercised, spraying may now be abandoned in other regions also. On the other hand, in another area where spraying is carried out, vectors are still occasionally found, and Pacifico (p. 132) considers it necessary to continue the control measures.

A full account of the attempt to eradicate *Anopheles* mosquitoes from Sardinia, particularly *A. m. labranchiae*, has been written by Logan (p. 1019). It became evident that eradication could not be achieved by spraying alone, and that chief reliance would have to be placed on larvicidal measures. At the end of the enterprise *A. m. labranchiae* had not been eliminated, but had been restricted to a few persistent foci, and malaria had almost disappeared. Aitken *et al.* (p. 1213) comment on the most recent surveys of Sardinia, noting that *A. claviger* and *A. algeriensis* have multiplied, the latter having taken over the breeding places of *A. m. labranchiae*, which has almost disappeared. *A. sacharovi* has reappeared after a long absence. Malaria continues to be extremely rare.

In Corsica the mixed spray and larvicidal campaign has virtually eliminated malaria and very markedly reduced *A. m. labranchiae* and *A. sacharovi*. Roubaud and Toumanoff (p. 1143) comment that female *A. maculipennis* tend to reject water surfaces which have been treated, and have been driven to breeding at higher altitudes. Sautet (p. 1224) notes that *A. sacharovi* is still found in places where it is exophilic in

habit. He discusses how the campaign should now be modified to reduce cost: it has not led, as was hoped, to an expansion of farming.

Belios (p. 346) reports on the malaria control work carried out in Greece from 1946 to 1952, which resulted in a great reduction in the incidence of the disease. The work was based on the use of DDT. Livadas (p. 1144), however, expresses the fear that after the phenomenal success of these campaigns, malaria is again showing an increase, probably because *A. sacharovi* is becoming resistant to insecticides, and Belios (p. 1144) amplifies this question of resistance, which seems to be definite. In comment Macdonald points out the desirability of direct measurements of resistance, which have not so far been made in Greece.

An extensive epidemic of malaria occurred in the Danube delta area of Rumania in 1941–44. Jírovec (p. 766) describes the organization developed to control it by means of drugs and residual insecticides.

Morin (p. 534) sums up the very extensive antimalaria work of WHO in the eastern Mediterranean region.

Bruce-Chwatt (p. 534) discusses the problems relating to the control of malaria in tropical Africa, making the point that a survey is an integral part of a control scheme. He gives figures of the cost of residual insecticide programmes, which are a continuing expense, and discusses the importance of balancing all forms of social and economic progress.

In Katanga, Belgian Congo, DDT spray is used once each year in the peripheral areas of major towns and along feeder roads to a distance of 20 kilometres, but the centres of these towns are not treated. Feuillat *et al.* (p. 767) report that these measures have been very successful, trapping experiments now showing that the vectors, *A. gambiae* and *A. funestus*, have fallen from 90 to 3 per cent. of the total catch. Parasite rates have fallen similarly. Comparable results are reported in a large mining industry, but in rural areas the situation is not so satisfactory.

In Southern Rhodesia control of malaria alternates with control of schistosomiasis according to the season of the year. Alves and Blair (p. 13) have found that 6 teams using BHC for residual spraying in the malaria (wet) season, and copper sulphate in the waters in which there is most contact between man and the snail hosts in the dry season, have been able to exercise a great measure of control. The intention is to extend this service. Mastbaum (p. 1226) shows that in Swaziland, where regular BHC spray has been carried out for several years, *A. gambiae* is kept out of the huts without being eradicated from the area. An epidemic recently occurred which was controlled by intensifying the spray campaign, and in this epidemic there was some indication that the population had partly lost its immunity.

In Madagascar a long and successful campaign in which DDT, BHC and Octochlor have been used (preferably together) is described by Bernard (p. 1037), who notes that chloroquine has also been employed for prophylaxis. The results have been good. *A. funestus* has disappeared from the plateau and is now rare elsewhere; *A. gambiae* is still present but is no longer important. The malaria indices and the general death rate have declined. A similar impressive record for Tananarive is given by Mercier and Razafindrakoto (p. 15).

In Réunion (p. 535) a DDT spray campaign has resulted in the almost total disappearance of anophelines from houses, but the opinion is expressed that *A. gambiae*, the only vector of malaria, cannot be eliminated without antilarval measures; it shows a growing tendency to resort to outdoor resting places. The DDT campaign has no effect on *Culex fatigans*.

In India much use is made of insecticidal spray in malaria control, and

Jaswant Singh *et al.* (p. 769) have compiled a review of the results of residual insecticide work in various oriental countries, giving dosages and frequency of application; Sharma and Rajindar Pal (p. 142) also report on DDT, BHC and dieldrin as used in India, giving details. These authors (p. 143) made a study of anophelines near Delhi, finding that a DDT suspension had a strong irritant-repellent effect which was not evident with an emulsion; BHC was moderately repellent for a short time.

Antilarval methods and suppressive proguanil have been abandoned in part of Uttar Pradesh where *A. culicifacies*, *A. fluviatilis* and *A. stephensi* are the vectors, and Srivastava and his colleagues (pp. 16, 881) now use DDT as a residual spray 4 times each year, with very good results. Similarly on plantations in the Madras State, where antilarval measures had at best been only moderately effective, Gilroy (p. 16) reports most successful use of DDT and BHC. There is little or no advantage in giving suppressive drugs as well. On the other hand Ananthaswamy Rao *et al.* (p. 768) argue that antilarval methods may still be suitable, and relatively cheap, for large communities, but that they are too expensive for small communities. They discuss the choice of methods.

Bhombore *et al.* (p. 882) report considerable general economic improvement in villages of Mysore in which DDT campaigns have been carried out, and simultaneous reductions in the spleen rates. The first year of extensive spraying operations in the Punjab resulted in considerable reduction in the incidence of malaria (Rafi, p. 768).

In the Annual Report of the Malaria Advisory Board, Malaya, (p. 758), it is stated that residual insecticides seem to be able to reduce greatly, but not to eliminate, transmission by *A. maculatus*; dramatic results are not expected, as other vectors are generally less readily killed than *A. maculatus*.

Ketterer (p. 465) describes the malaria control measures taken in Indonesia, where DDT has been used to reclaim valuable rice-growing and other areas from malaria. He mentions the consequent increase in production and reduction in hospital expenses. In N. Borneo the vector is *A. balabacensis* [*A. leucosphyrus*], which breeds in shade and enters houses at night, resting before and after feeding and before leaving. McArthur (p. 17) evolved a method of control by admitting sunlight to the breeding places, and Colless (p. 346) has experimented with DDT in kerosene as a house spray. The periods of resting were much reduced on surfaces treated with DDT and kerosene, but increased as the effects wore off.

Adan (p. 768) in the Philippines has shown that *A. minimus flavirostris* is amenable to control by residual insecticides.

In Trinidad the dangerous vectors are *A. aquasalis* and *A. bellator*; the control programme includes cleaning, drainage and larvicidal work, a DDT house-spraying programme, and (for *A. bellator*) the use of copper sulphate for the bromeliads in which breeding occurs. Gillette (p. 19) shows that malaria has been greatly reduced. Dieldrin has also been used, as a larvicide in the form of a wettable powder, and in oil. The powder gave adequate control for at least 14 days, and the oil was as effective as similar preparations of DDT (Gillette and Gilkes, p. 1038).

In Central America, where *A. albimanus* is the vector, DDT residual spray has been very successful. Owens (p. 18) and (for Costa Rica) Peña Chavarría and Guerrero Arguedas (p. 536) report excellent results.

In British Guiana (p. 347) a DDT-xylol emulsion is largely preferred to other preparations for residual spray. The incidence of malaria is now extremely small, the birth rate has risen by one-third since 1943, the death rate and the infant mortality rate have fallen dramatically. *A. darlingi* is

not now found but larvae of *A. aquasalis* and *A. albitarsis* are still fairly numerous. The DDT programme has now no sustained effect against *C. fatigans*. In French Guiana Floch (p. 348) reports marked reduction in malaria in 1951, after several years of DDT spray campaigns. *A. darlingi* is not now found, though *A. aquasalis* remains very prevalent.

In Ecuador the vectors are *A. albimanus* along the coast, and *A. pseudopunctipennis* in the valleys of the Andes; the latter and *A. punctimacula* are subsidiary vectors on the coast. DDT programmes have been carried out since 1949, but Montalván (p. 466) estimates that remaining foci will not be eliminated until 2 more years of intensive effort have been completed.

In the State of São Paulo, Brazil, there has in recent years been a remarkable decline in the prevalence of malaria. DDT has been used on a very large scale since 1946, but Unti and Coda (p. 349) report that it is not easy to evaluate the rôle it has played because the results have been discordant. It has given good results against *A. tarsimaculatus* and *A. albitarsis*, disappointing results against the *Kerteszia* group, and variable results against *A. darlingi*.

Copper sulphate is usually employed to kill the bromeliads in which anophelines of the subgenus *Kerteszia* breed; Aragão (p. 19), however, has successfully used paris green dusted from aircraft for the purpose, but the dose (2·5 gm. per square metre) is high.

Chemotherapeutic Research

Parasites of animals are much used in chemotherapeutic research, and it is convenient to record this work separately. Cortisone has been tried, and although Singer (p. 1040) found that in mice infected with *P. berghei* it led to longer survival and lower degrees of parasitaemia than in controls, Schneider (p. 764) and Roberts (p. 885) were not able to demonstrate any marked effect. Schneider's results were similar in *P. gallinaceum* and *P. vivax* infections. No significant action of cortisone on the course of infections with *P. gallinaceum*, or on the immunity provoked, could be detected by Grignaschi (p. 540).

Siddons (p. 147) describes methods used for screening antimalarial drugs. Blood-induced *P. berghei* infections react to drugs like similarly induced *P. vivax* and *P. falciparum* infections, but the mechanism of cure is different. He gives results obtained with many different substances.

Thurston (p. 148) has studied drug resistance in *P. berghei*. Strains resistant to sulphadiazine and pyrimethamine are cross-resistant to drugs which affect the dividing nucleus of the parasite.

The relationship between folic acid and the action of various drugs has been mentioned by several authors. Thurston (p. 885) states that the action of proguanil, pyrimethamine and certain other drugs on *P. berghei* is antagonized by PAB and folic acid, and discusses the possibility that these drugs may have similar actions. Bishop (p. 888) observed that in *P. gallinaceum* made resistant to certain drugs—all antagonists of PAB or folic acid—a large number of gametocytes are produced, but not, apparently, by direct action of the drugs. The phenomenon may be related to the fact that folic acid is concerned in the synthesis of nucleic acid. Greenberg (p. 1229) shows that certain analogues of folic acid can reverse the antimalarial effect of sulphadiazine, possibly by serving as a source of folic acid for the parasite (*P. gallinaceum*). On the other hand, in a study of the mode of action of proguanil and related compounds on *P. gallinaceum* Ryley (p. 351) found that their effect could not be reversed by folic acid

or thymine, which led him to think that the parasites cannot use folic acid as such, but that purines and pyrimidines must be in the form of nucleosides or nucleotides for incorporation into parasite nucleic acid.

In studying the action of drugs on the erythrocytic forms of *P. gallinaceum*, Josephson *et al.* (p. 469) put forward a hypothesis to the effect that drugs which inhibit the parasite during active reproduction are probably analogues of normal metabolites, and resistance to them can readily be produced, but that those which inhibit the parasites at all stages of development are probably not analogues of natural metabolites, and resistance cannot readily be produced.

Krishnaswami *et al.* (p. 773) show that certain metabolites of proguanil are active against *P. berghei* as they are against *P. gallinaceum* and *P. lophurae*. A metabolite of bromguanide, isolated from the urine of monkeys, proved to be exceptionally active against *P. gallinaceum* but less so against *P. knowlesi* (Bami, p. 776).

Jaswant Singh *et al.* (p. 149) by feeding mosquitoes infected with *P. gallinaceum* on glucose solution containing proguanil or pyrimethamine, have shown that these drugs exert a prophylactic action in the invertebrate as well as in the vertebrate host.

Jaswant Singh *et al.* (p. 679) describe their methods of assaying antimalarial drugs against *P. gallinaceum*. On this basis the activity of pyrimethamine was found to be high. The curative and prophylactic activity of pyrimethamine against *P. gallinaceum* has been studied by Greenberg and his colleagues (p. 354), who found it considerably more active than proguanil and quinine. It can sterilize sporozoite-induced infections and eradicate pre-erythrocytic forms, but cannot eradicate established erythrocytic infection. They (p. 1228) show that a large dose of pyrimethamine given on the 7th day of a sporozoite-induced infection with *P. gallinaceum* (strain B1, which normally gives a wholly exo-erythrocytic type of fatal infection) prevents death from exo-erythrocytic forms (such as usually occurs), and gives time for pigmented blood forms to develop. They (p. 1228) discuss the time of administration, dose and prophylactic activity of pyrimethamine on sporozoite-induced *P. gallinaceum* infections.

Jaswant Singh *et al.* (p. 776) quote experiments which indicate that *P. gallinaceum* rendered resistant to pyrimethamine may retain this property in the pre-erythrocytic forms, as has been shown to be the case with proguanil.

Baranger and Filer (p. 1146) discuss the antimalarial action of simple mineral or organic substances on *P. gallinaceum*.

Considerable activity has been found in tests of dihydrotriazines against *P. lophurae* and *P. berghei* (Hewitt *et al.*, p. 775).

Mudrow-Reichenow (p. 149) has tested primaquine and pamaquin on gametocytes of *P. cathemerium* and other parasites; and on their development in mosquitoes. Both were active against gametocytes, and mosquitoes fed on infected birds 17 hours after treatment with primaquine failed to develop oöcysts (though controls did so); results were not so good 43 hours after treatment. When mosquitoes were fed on sugar water with primaquine, invasion of the salivary glands by sporozoites was prevented.

A study of the action of chloroquine, proguanil, pyrimethamine, pentaquine and isopentaquine on *P. hexamerium* is reported by Manwell and Khabir (p. 1146).

The minimum effective doses of chloroquine diphosphate, chloroquine sulphate and amodiaquine for monkeys infected with *P. cynomolgi* were found to be 1·5, 1·0 and 3·5 mgm. per kgm. respectively (Jaswant Singh *et al.*, p. 772).

Nathan and Cowperthwaite (p. 889) have used the trypanosomid flagellate *Crithidia fasciculata* for evaluating antimalarial drugs.

Plasmodia of Monkey Malaria

Bray (p. 883) gives an account of the exo-erythrocytic part of the life cycle of mammalian malaria parasites. Shortt *et al.* (p. 883) have now been able to describe pre-erythrocytic schizonts of *P. cynomolgi* 2, 3 and 4 days old, and also schizonts of 15, 17 and 105 days old.

Experiments on mixed infections showed that *P. cynomolgi* tends to suppress *P. inui* except in splenectomized animals (Jaswant Singh and Ray, p. 1145).

Edeson and Davey (p. 19) have isolated a fresh and virulent strain of *P. knowlesi* from a monkey in Malaya, and Jaswant Singh *et al.* (p. 20) describe the effects of this strain in rhesus monkeys. Edeson (p. 20) has found in the livers of monkeys infected with this strain bodies which he takes to be exo-erythrocytic stages of *P. knowlesi*, and points out their resemblance to similar stages in *Hepatocystis kochi*. In comment Garnham suggests that these large bodies are not likely to be pre-erythrocytic forms, which could hardly have reached the size indicated in the prepatent period which Hawking and Mellanby (p. 21) have shown may be as short as 8 days. The forms may be post-mature "giant" schizonts such as have been described in *P. cynomolgi*.

Plasmodium berghei

Much work has been carried out on *P. berghei*. Vincke and his colleagues (p. 536) have written a general survey of such research, and (p. 350) have compiled a list of mammals susceptible to this parasite [certain African bats may be included (Rodhain, p. 144)] and to *P. vinckei*.

Greenberg *et al.* (p. 350) have observed differences in the course of infection with *P. berghei* in mice of different strains, and according to sex; and the existence of natural immunity in certain individual white mice has been demonstrated by Matilla *et al.* (p. 772); it was overcome by splenectomy.

Immunity has been studied by Fabiani and Fulchiron (p. 146), who show that serum from rats hyperimmunized by superinfection had some protective action when injected into clean rats before infection, but that it was brief and acted only by inhibiting infection for a few days. Parasitized erythrocytes inoculated intraperitoneally into immune animals were subjected to rapid macrophage phagocytosis. The mechanism of immunity is cellular and the immune serum seems to have an opsonic action. Krishnaswami *et al.* (p. 539) attempted to estimate the immunity acquired by blood infection of white rats. It is evidently powerful, but could not be measured accurately. Superinfection with *P. berghei* reveals marked immunity in previously infected voles, even if the spleen is removed when the infection has become chronic or cured, and some weeks are allowed to elapse before superinfection. In voles which have recovered at the time of splenectomy and are then superinfected, some die and some pass to a chronic or latent state, indicating variations in the degree of immunity (Zuckerman, p. 252).

Bruce-Chwatt (p. 884) shows that congenital *P. berghei* infection is most exceptional, and must be due to mechanical or functional deficiency in the placenta. Experiments indicated that immunity is transmitted from mother rat to young by the milk.

P. berghei shows a predilection for reticulocytes (Singer, p. 1040) whose numbers control the degree of parasitaemia, and which greatly increase

in the acute phase of infection and in relapse (Ramakrishnan *et al.*, p. 539). The metabolism of reticulocytes was investigated by Sherwood Jones *et al.* (p. 537).

Metabolic studies are reported by Whitfeld (pp. 22, 537) who investigated the nucleic acids of *P. berghei* and its uptake of radio-active phosphorus.

In white rats the decrease in liver glycogen during the course of infection reflects a true disturbance of liver function (Mercado and von Brand, p. 1039).

Pérez-Reyes (p. 467) found *A. albimanus* insusceptible, *A. quadrimaculatus* temporarily but not permanently susceptible, and *A. aztecus* continuously susceptible to *P. berghei* in experiments lasting several months. The best time to infect *A. aztecus* was on the 5th and 6th days after blood inoculation of the hamsters on which they fed. Box *et al.* (p. 22) show that *A. quadrimaculatus* is not a good vector.

Ramakrishnan *et al.* (p. 467), using many species of mosquitoes, failed in many attempts to transmit *P. berghei* by bite (except that sporozoites were found once in *A. stephensi*), although they found both male and female gametocytes in the blood of the animal hosts when the mosquitoes were allowed to feed. In comment Garnham suggests that there may have been errors in diagnosis of the gametocytes, and suggests that the experiment might have been more successful if the feeding had taken place early in the infection, irrespective of gametocyte density.

Infection of animals by ingestion of blood infected with various malaria parasites has been reported by different workers; Beltrán and Amanda Reyes (p. 21) now record success with *P. berghei* and white rats.

The Henry reaction in rats infected with *P. berghei* is positive soon after infection, and becomes negative 3 or 4 months after cure—at about the time when premunition ends (Fabiani *et al.*, p. 147). A complement-fixation reaction which gave positive results is described by Pautrizel and Nguyen-Vinh-Nien (p. 540); the titre was high in hyperimmunized rats.

In experiments on white mice infected with *P. berghei*, Box *et al.* (p. 774) showed that when treatment (with various drugs) was delayed for several days after infection there were fewer cures than when it was begun at once. They tested a number of compounds under standard conditions with the object of assisting the estimation of their effects on *P. vivax* infections.

Diet and Infection with Malaria Parasites

In starving albino rats the growth of *P. berghei* is suppressed. Ramakrishnan (p. 145) shows that in this phase a degree of immunity develops, and with his colleagues (p. 773) shows that administration of methionine or PAB to starved rats can cause growth of *P. berghei* comparable with that in controls on normal diet. Similarly, in rats on a special diet of amino acids with fats and carbohydrates, parasitaemia occurred if methionine and *p*-hydroxybenzoic acid were added, but not always with PAB. Fulton (p. 468) shows that rats on a milk diet were not susceptible to *P. berghei*, but became so if cortisone was given each day.

The subject of milk and protection against malaria has attracted considerable attention. Jaswant Singh *et al.* (p. 884) show that a milk diet protects monkeys against *P. knowlesi* but does not completely sterilize the infection; little or no premunition develops. Rats on an exclusively milk diet showed milder infection with *P. berghei* than controls (Ramakrishnan *et al.*, p. 145).

Schneider and Montézin (p. 772) show that milk without the addition of vitamins B1 and B6 and calcium pantothenate does not protect against large inocula of *P. berghei*, and Mackerras (p. 21) also gave vitamins of the B group in addition to milk to produce the protective effect. Both Hawking (p. 538) and Rodhain (p. 468) have shown that the protective action of milk can be reversed by PAB.

Protection against *P. vinckei*—and to a smaller extent against highly virulent strains of *P. berghei*—was demonstrated by Rodhain (p. 144), who shows, however, that *Babesia rodhaini* is not inhibited in this way; nor is *Trypanosoma lewisi* (Mackerras, p. 21). The metabolic requirements of these parasites may be different.

On the other hand, a milk diet caused a more intense and fatal parasitaemia in fowls infected with *P. gallinaceum*. Ramakrishnan *et al.* (p. 887) show that gametocytes from such birds were infective to mosquitoes.

Plasmodia of Bird Malaria

Ball (p. 1229) has been able to maintain the isolated gut of a mosquito alive for 5 weeks in an elaborate synthetic medium; oöcysts, however, did not develop in this medium for more than 4 or 5 days, but the method may be useful for studies on the development of plasmodia.

Huff (p. 1145) discusses the fact that various malaria parasites of birds develop at first in the spleen and later in endothelial cells of other organs. This conversion of host-cell preference is probably the result of mounting immunity in the spleen cells. Verolini (p. 148) has shown that exo-erythrocytic forms of *P. gallinaceum* can develop in tissue culture of splenic tissue from fowls inoculated with erythrocytic parasites, but could not decide whether these forms arose from EE stages already present in the splenic culture, or from the erythrocytic parasites.

Terzian (p. 469) shows that X-radiation can increase the innate resistance of *Aëdes aegypti* to *P. gallinaceum*, but that this can be reversed by administration of penicillin or sulphadiazine to the irradiated mosquitoes before infection.

By infecting chicks with sporozoites of *P. gallinaceum* taken from mosquitoes at different times after infection, Porter *et al.* (p. 1041) have shown that infectivity declines according to length of residence in the salivary glands.

A study of a mixed infection of chicks with 2 strains of *P. gallinaceum*, each with marked characteristics, is reported by Greenberg and Trembley (p. 1227).

In an examination of the amino acids of the blood in *P. gallinaceum* infections, Rama Rao and Giri (p. 775) found a marked increase in glutamic acid.

Micks and McCollum (p. 150) were able to infect *A. quadrimaculatus* with *P. cathemerium*, but although the oöcysts reached maturity, the sporozoites never appeared in the salivary glands.

Phanerozoites of *P. lophurae* in turkeys are reported by Manresa (p. 23).

McGhee (p. 23) has studied the infection with *P. lophurae* which takes place in washed duck erythrocytes inoculated into chick embryos which have previously been infected with that parasite.

Schwink (p. 886) made the interesting observation that chickens could be passively protected against *P. lophurae* infection by plasma from chickens immunized with red cells of the same species, in the absence of malaria infection. The protection afforded by the plasma of chickens immunized against *P. lophurae* was much less effective.

Perez Reyes and Peláez (p. 253) describe the properties of a strain of *P. relictum*, and David and Krishnan (p. 541) show that pigeons in Delhi are not susceptible to the local strain. The consumption of glucose by *P. relictum* is greater than the consumption by reticulocytes or mature red cells (Warren and Manwell, p. 541).

Laird (p. 24) writes on *P. vaughani* and the exo-erythrocytic schizogony of the *elongatum* type which occurs in this species.

Huff (p. 24) contributes a study of *P. huffi*, a parasite of toucans.

Ray *et al.* (p. 24) describe a species of *Plasmodium* in Indian partridges.

Charles Wilcocks

MALARIA

In this section abstracts are arranged as far as possible in the following order:—Human malaria—*epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control;* Animal malaria—*monkeys, other animals, birds.*

See also p. 415, India. **Report of the Malaria Institute of India for the Years 1948–1950.**

Venkat Rao, V. **Malaria Vectors of India. V.** *A. annularis* **Van der Wulp, 1884.** *Bull. Nat. Soc. India for Malaria & other Mosquito-Borne Dis.* 1954, Nov., v. 2, No. 6, 191–9. [19 refs.]

Anopheles annularis is widely distributed in India and the Far East, but it is an important vector of malaria only in the coastal region of Orissa (India).

The present paper is more in the nature of a review of the work done on the breeding places, habits and control of this mosquito; however, particular aspects of its biology and control, which may be investigated further, are referred to. For example, mention is made of the lack of information on outdoor resting places and longevity of *A. annularis* in India.

It is suggested by the author that climatic conditions in Orissa may result in " gonotrophic discordance " in these mosquitoes, a term denoting that the females require more than one blood meal for maturing the eggs [this *Bulletin*, 1948, v. 45, 137]. As a result they may be found inside houses or cattlesheds for sufficiently long periods to show infections of the salivary glands. In other parts of India where climatic conditions are different, it would appear that the females are obliged to leave the shelters of houses and cattlesheds for oviposition after a single blood meal and may therefore be short-lived. This probably would explain why *A. annularis* is not an important vector in these places.

With regard to control of the species in rural areas, the author refers to the present-day high cost of labour involved in clean-weeding of the breeding places, and the cultivators' objections to treating their rice fields with paris green. The best method of control, therefore, would be to treat houses and cowsheds with DDT during June–July, before the start of the malaria season which lasts from August to November. In larger towns where breeding places are relatively few, clean-weeding of the breeding places and improved methods of rice growing, might effectively control the mosquito.

M. G. R. Varma

Crandell, H. A. **Resistance of *Anopheles sundaicus* to DDT. A Preliminary Report.** *Mosquito News.* 1954, Dec., v. 14, No. 4, 194–5.

In the coastal area of Djakarta and in Tjirebon, a city 200 km. away, reports of mosquitoes surviving in houses sprayed with DDT indicated the possibility of DDT-resistance. The mosquitoes were found to be *Anopheles sundaicus*, the principal malaria vector. If this resistance is proved, it might explain the failure of DDT spraying to control the malaria which has only shown a very small decline after 2 years of spraying.

Laboratory tests were done with wild-caught mosquitoes exposed to sprayed panels for 30 minutes and afterwards kept in clean cages. These tests showed that *A. sundaicus* mosquitoes from treated areas were 20 to 30 times as resistant as those from untreated places. The DDT-resistant strain showed no abnormal tolerance of dieldrin and, accordingly, further house spraying will be done with this insecticide, at a rather high dosage (0·5 gm. per sq. m.). *J. R. Busvine*

Jones, J. C. **Some Notes on the Behaviour of Fourth Instar *Anopheles quadrimaculatus* Say (Diptera, Culicidae).** *Mosquito News.* 1954, Dec., v. 14, No. 4, 186–91, 5 figs. on pl. [13 refs.]

This is a qualitative descriptive list of 14 different types of behaviour and activities of normal fourth-stage larvae of *Anopheles quadrimaculatus* based on macroscopic and microscopic observations made over a period of 4 years on larvae in laboratory colonies; it includes such activities as feeding, diving, swimming, etc. A plate illustrates diagramatically some of the attitudes assumed in, for example, browsing and cleaning activities.

H. S. Leeson

Barr, A. R. **Hybridization Experiments with some American Dark-Winged Anophelines.** *Exper. Parasit.* New York. 1954, Sept., v. 3, No. 5, 445–57.

"Three closely related species of mosquitoes, *Anopheles quadrimaculatus*, *A. freeborni*, and *A. aztecus*, were reciprocally hybridized.

"Hybridizations between *A. quadrimaculatus* and either *A. freeborni* or *A. aztecus* resulted in a reduction in the numbers of eggs laid, of which reduced percentages hatched. Practically all the hybrids died in early larval life; only rarely did they develop as far as the third larval instar. Only one adult was produced in these crosses and it was shown to be fertile by back-crossing.

"Crosses involving *A. aztecus* and *A. freeborni* also resulted in reduced numbers of eggs being laid of which reduced numbers hatched but the reductions were not so striking as when either of these forms was crossed with *A. quadrimaculatus*. The hybrid larvae were not so vigorous as normal ones but large numbers of adults emerged. Fertile F_1 females were produced no matter which female parent was used but a normal percentage of hybrid males was produced only when *A. freeborni* was the female parent; when *A. aztecus* was the female parent, only a small proportion of the progeny was male. In the former case, fertile males were produced but in the latter they could not be tested.

"The patterns of the hybrid eggs were similar to those of the females which laid them in those cases where they were observed.

"These results support the conclusions derived by studies of morphology, that *A. aztecus* and *A. freeborni* are more closely related to each other than

either is to *A. quadrimaculatus* and that the differences among the three forms are large enough so that they may be considered to be specifically distinct."

WHITE, L. G. & DOERNER, A. A. **Functional and Needle Biopsy Study of the Liver in Malaria.** *J. Amer. Med. Ass.* 1954, June 12, v. 155, No. 7, 637–9. [Refs. in footnotes.]

The following liver function tests were carried out in 37 cases of malaria (19 *P. falciparum*; 14 *P. vivax*; 2 *P. malariae*; 2 unidentified): cephalin-cholesterol flocculation, thymol turbidity, *gamma* globulin turbidity, zinc sulphate turbidity, bromsulphthalein excretion, serum bilirubin, prothrombin time, total protein and A/G ratio, serum cholesterol and cholesterol esters. Biopsy specimens of liver were obtained in 3 cases of *P. falciparum* and 4 of *P. vivax* malaria. Deviations of most function tests were observed, which returned to normal after antimalarial treatment. The biopsy material disclosed little change beyond pigment in the Kupffer cells and eosinophils [whereabouts not stated].

The authors conclude that the abnormalities in " function " tests probably arose from involvement of the reticulo-endothelial system. There was no evidence of chronic hepatitis following malarial infection.

[Important details are missing from this paper in regard to biopsies. The severity of the relevant infection, its duration before treatment, and the method of treatment are not detailed. The meaning of " after treatment " is not defined, so that the all-important time factor cannot be assessed.] *B. G. Maegraith*

EDINGTON, G. M. **Cerebral Malaria in the Gold Coast African: Four Autopsy Reports.** *Ann. Trop. Med. & Parasit.* 1954, Sept., v. 48, No. 3, 300–306, 2 figs. on pl.

The autopsy and histopathological findings in 4 children who died of cerebral malaria in Accra (Gold Coast) are recorded. In general the findings corresponded to those recorded by other observers of similar forms of malignant malaria.

In the livers of all 4 children there was much malarial pigment in the Kupffer cells. In one, scanty granules containing free iron were present in the periportal parenchymal cells. In the other 3 no free iron was detected. No free iron was found in two spleens; the other two contained only traces. The author states that absence of iron-containing pigment is usual in " chronic " malaria in children in the Gold Coast. Haemosiderosis is, however, common in the adult on the Gold Coast, which suggests that the iron content of the diet is high. He goes on to say that " in neither cerebral nor chronic malaria in the Gold Coast is an iron-containing pigment demonstrable in the tissues " [a statement to some extent controverted by the findings described in the paper].

The author states that the pigment in the liver in young children is most obvious in the Kupffer cells, with relatively little in the portal tracts. In older children this deposition arrangement tends to be reversed. Finally, there is pigment in the portal tract only. He regards the presence of pigment in the portal tract as evidence of malarial infection of some duration.

The cases described were treated before death. In 3, only a few parasites were seen in the blood vessels of the various organs examined, though they

were present in ring haemorrhages in the brains of 2 patients, and malarial granulomata were found in the third. A negative blood slide does not therefore necessarily exclude a diagnosis of cerebral malaria "if there is any possibility of previous treatment". This was well illustrated in one autopsy in which the peripheral blood vessels contained no parasites although in the brain malarial granulomata containing parasites were present.

[The relative scarcity of free iron-containing pigment in liver tissues has also been noted in animals, and was referred to in an earlier communication by this author. His findings in the spleen are surprising in view of the great preponderance of free iron-containing pigment in that organ in mammalian malaria, even in animals in which the pigment in the liver is almost entirely malarial.] *B. G. Maegraith*

Dimson, S. B. **Congenital Malaria in England.** *Brit. Med. J.* 1954, Nov. 6, 1083–5. [21 refs.]

The case described is of a woman aged 24 who travelled to England from Nigeria when 5 months pregnant. The period elapsing between return to Britain and delivery is not stated but the child at birth weighed 6 lb. 11½ oz. and so presumably was born near term. Jaundice, fever and vomiting occurred within the first 48 hours of extra-uterine life. A diagnosis of congenital infective hepatitis was made and the infant was treated with 250 mgm. aureomycin every six hours. After four days of this treatment slight improvement only had occurred; a chance remark then made by the mother led to blood films being examined and to the demonstration of a *Plasmodium falciparum* infection in mother and infant. The infant was at first treated with mepacrine by mouth but because vomiting was excessive this was replaced by pyrimethamine. Two months later it was considered probable that the infant was still infected although parasites could not be found in the blood. A further course of pyrimethamine was given and subsequent progress was apparently uneventful.

The author proceeds to discuss the efficacy of aureomycin, mepacrine and pyrimethamine in such cases. [The most important lessons to be drawn from the case, however, are that the recent movements of all patients should be enquired into as a routine in history taking, and secondly that cases of tropical illness should be referred to a centre equipped and staffed for the purpose.] *A. W. Woodruff*

Bruce-Chwatt, L. **Mepacrine and Malaria in Children.** [Correspondence.] *Brit. Med. J.* 1955, Jan. 22, 226.

The author refers to Dimson's paper on congenital malaria [above] and his own report of the toxic effects of intramuscular mepacrine in small children, published 4 years ago [this *Bulletin*, 1950, v. 47, 956].

He now reports from Nigeria the case of a European baby of 6 months who was treated with 50 mgm. of mepacrine musonate intramuscularly for a symptomless fever, despite persistently negative blood films. Within 20 minutes of the injection, the infant developed toxic and clonic convulsions, cyanosis and collapse. The patient was given nikethamide, artificial respiration and a large dose of chloral, oxygen and cardiac stimulants; the chloral and oxygen had to be kept up for several days because of repeated clonic

convulsions. The temperature rose to 104°F., but no abnormalities were found in the cerebrospinal fluid.

With careful treatment the fever and convulsions abated within a week, except for occasional twitchings of the limbs and bouts of muscular rigidity. The skin was yellow and mepacrine was excreted in the urine for several days.

After discharge from hospital the child showed impairment of head control and some hypotonia; two months later, there was failure to sit up and feeble grasp but no major abnormality. There was a slightly raised protein content in the fluid. A year later the child still had partial paralysis of one arm, evidence of spastic paraplegia in the legs and appeared to be mentally retarded.

While such cases are uncommon, the author suggests that intramuscular administration of mepacrine to infants might well be more critical: he suggests the use of chloroquine which is much better tolerated by all age-groups. *H. J. O'D. Burke-Gaffney*

i. Soberón y Parra, G. Estudios sobre el Daraprim en infecciones experimentales por *Plasmodium* de aves y en casos humanos de paludismo causado por *Plasmodium vivax*. [**Studies on the Activity of Daraprim in Experimental Infections with Avian Malaria and in Human Infections with** *Plasmodium vivax*] *Bol. Epidemiológico*. Mexico. 1953, Jan.–Feb.–Mar., v. 17, No. 1, 10–16, 1 graph. [25 refs.]

ii. ——— ———. Observaciones sobre los resultados obtenidos con el "Daraprim" en el tratamiento de 92 casos de paludismo por *P. vivax* en Villahermosa, Estado de Tabasco. [**Results obtained with Daraprim in the Treatment of 92 Cases of** *P. vivax* **Malaria in Villahermosa, Tabasco State**] *Bol. Epidemiológico*. Mexico. 1953, Jan.–Feb.–Mar., v. 17, No. 1, 17–18, 1 chart.

These two papers by the Director General of the Mexican National Campaign against Malaria describe work carried out by members of his staff, in collaboration with the Organization for Interamerican Public Health Cooperation, to evaluate the antimalarial activity of Daraprim (pyrimethamine).

i. Young adult pigeons (*Columba livia*) were grouped in lots of five. After they had been kept under observation for a week each bird was inoculated with a strain of *Plasmodium relictum*, by the intravenous injection of 25 million red cells of infected blood. Forty-eight hours after infection the administration of Daraprim was begun. Birds of five lots were given daily doses of 0·1, 0·2, 0·4, 0·8 and 1·6 mgm. per kgm. body weight, respectively, for five days. The daily dose was given in two portions with a six-hour interval. The drug was given by mouth by means of a syringe and a tube.

Daraprim acted as a suppressive: the minimum effective daily dose was 0·4 mgm./kgm., 2 mgm. per kgm. in all. One bird which had received 0·8 mgm./kgm. a day for 5 days relapsed 43 days after the end of treatment. The chief action of the drug appeared to be against erythrocytic dividing forms of the parasite: it had little effect, if any, on exoerythrocytic forms. Death of the birds appeared to be due to anaemia caused by the infection and not to the activity of exoerythrocytic parasites.

A similar experiment was carried out with 8 four-week-old chicks, two of which were untreated controls, infected with *Plasmodium gallinaceum*. The technique used was as described above. Three chicks received daily

doses of 0·8 mgm. and three 1·6 mgm. per kgm. body weight for five days. The smaller doses prolonged the life of the birds: from the 8th to the 12th day after infection there was no apparent parasitaemia, in contrast to the two control birds which died with excessive parasitaemia on the 6th day after infection. The 0·8 mgm./kgm. chicks began to show a few parasites in the blood from the 17th day after infection: these increased rapidly and one bird died 5 days after the relapse caused thereby. With the 1·6 mgm. doses the first relapse occurred 20–23 days after infection. One died on the 27th day as a result of this relapse. The other two survived relapses which lasted 10 and 12 days respectively. Second relapses occurred some two weeks later after a parasite-free period. The second relapses were much milder, with few parasites. Both chicks were alive and parasite-free 63 days after infection. The doses of Daraprim used appeared to have only suppressive action: they did not prevent relapse. There was no indication of drug intolerance.

ii. In the Malaria Dispensary at Villahermosa, Tabasco State, 92 patients suffering from *P. vivax* malaria were treated with Daraprim by mouth, the dose for adults being 50 mgm. the first day and 25 mgm. on the second and third days. Young patients up to the age of 15 received proportionally smaller doses. The patients are classified in 3 groups: 68 with one parasite per microscopic field, 12 with 2 to 5 parasites; 12 with more than 5. In the first group parasites and symptoms disappeared after the first dose in 41 patients. In 22 others there were neither parasites nor symptoms on the third day. The infection of only one patient was resistant to the drug: he was treated with Camoquin 9 days later. In the second group the results were very similar but parasites and symptoms persisted slightly longer. One patient, free from parasites and symptoms 48 hours after treatment, relapsed 10 days after end of treatment: he was cured with Nivaquine [chloroquine]. In the third group 10 patients were free from parasites and symptoms 4 days after beginning treatment. The infections in the remaining two patients were absolutely resistant to Daraprim. In no case was there any sign of drug intolerance nor was any relapse noted during a subsequent period of observation which extended up to 100 days.

Norman White

Dern, R. J., Beutler, E. & Alving, A. S. **The Hemolytic Effect of Primaquine. II. The Natural Course of the Hemolytic Anemia and the Mechanism of its Self-Limited Character.** *J. Lab. & Clin. Med.* 1954, Aug., v. 44, No. 2, 171–6, 4 figs.

Primaquine in doses of 30 mgm. (base) daily was administered continuously to six Negro volunteers known to be sensitive to the drug. In all of them an acute lytic reaction occurred which was followed by spontaneous return of haemoglobin to control values in spite of continued administration of the drug. Haemoglobin levels began to fall within 3 to 5 days of the first administration of the drug; the maximum depression occurred between days 7 and 9. The original value for haemoglobin levels was reached again between days 20 to 30. Little change was noted after this time. White blood cells were not affected.

Six days before the administration of the drug commenced a sample of blood from a primaquine-sensitive subject was removed, labelled with ^{51}Cr and re-injected. The survival rate of the labelled cells was determined at intervals during administration of primaquine before and during the lytic phase. Subsequent to the haemoglobin reaching normal values, a further sample of blood was removed, labelled with chromium and re-injected.

Marked haemolysis of labelled cells occurred during the acute lytic phase. Beyond the point at which the minimum haemoglobin concentration was reached there was an abrupt decrease in the rate of haemolysis of labelled cells. In the stage of equilibrium, *i.e.* when the haemoglobin concentration had become approximately normal, the slope of the survival curve was normal.

Erythrocytes from primaquine-sensitive persons were labelled with ^{51}Cr and injected into a series of volunteers, each of whom had received 30 mgm. of primaquine base for varying lengths of time prior to the injection. The drug was continued after the transfusion of labelled cells and the survival curve of the latter determined. The labelled sensitive cells were haemolysed in all recipients who were given primaquine. In the sensitive persons who were in the equilibrium phase the capacity to haemolyse the sensitive cells was unaffected. The authors conclude that the reduction in haemolytic rate which occurred in the recovery phase could not be explained by any change in haemolytic capacity. Blood from a sensitive subject in the equilibrium phase was labelled with ^{51}Cr and re-injected into the donor and into a non-sensitive subject. The drug was continued in the donor and started in the recipient. The cells were haemolysed at the same rate in each case, demonstrating that the decreased rate of haemolysis observed in the earlier experiments after the minimum haemoglobin concentration had been reached appeared to be related to a reduced primaquine sensitivity of the cell. The authors suggest that this might be due either to the development of tolerance following exposure to the drug or to the elimination of susceptible members of the red-cell population.

It is interesting to note that prolonged administration with 30 mgm. daily produced no other evidence of toxicity. [For Part I of this study, see this *Bulletin*, 1954, v. 51, 676.] *B. G. Maegraith*

Beutler, E., Dern, R. J. & Alving, A. S. **The Hemolytic Effect of Primaquine. III. A Study of Primaquine-Sensitive Erythrocytes.** *J. Lab. & Clin. Med.* 1954, Aug., v. 44, No. 2, 177–84, 2 figs. [19 refs.]

The properties of erythrocytes of primaquine-sensitive persons were compared with those of non-sensitive persons. No significant differences could be detected between them, either before or during primaquine administration, except that Heinz bodies appeared just before and at the beginning of haemolysis in sensitive subjects and disappeared soon after haemolysis had started, whereas they were rarely seen in normal non-sensitive persons. The examination of the erythrocytes included the study of their morphology in wet and dry preparations, the Coombs test, electrophoretic analysis of haemoglobin and osmotic and mechanical fragility. A concentration of 0·1 mgm. primaquine per 1·0 ml. whole blood failed to cause haemolysis of either sensitive or non-sensitive cells after 48 hours' incubation.

B. G. Maegraith

Miller, M. J. **Milk Diet and Human Malaria.** *Amer. J. Trop. Med. & Hyg.* 1954, Sept., v. 3, No. 5, 825–30, 2 figs.

These experiments were carried out in Liberia on 9 African children. Group A consisted of 6 children in whose peripheral blood malaria parasites were present from the beginning of the experiment. Three showed *P.*

falciparum, two a mixture of *P. falciparum* and *P. malariae* and one *P. malariae* only. The second group (B) consisted of 3 children in whose blood parasites were absent at the beginning of the experiment but appeared later. One child had a mixed infection of *P. falciparum* and *P. malariae*, and the other two *P. malariae* only.

Group A received a normal diet for the first 8 days, milk and sugar only for the next 21 days, after which the normal diet was restored for 21 days and followed by a further period of 21 days on milk and sugar. In the latter period they received a yeast supplement for 10 days. Group B received a normal diet for the first 50 days followed by a period of 21 days on milk and sugar only. The normal diet was supplemented by yeast on two occasions for periods of 14 and 10 days respectively. The children were isolated and kept under supervision day and night over the whole period. The parasite density was determined daily for each child.

Within the conditions of the experiments it was found that a milk diet, or the addition of yeast to a normal diet did not influence the parasite density or the clinical picture. The author points out that the results of this experiment are not strictly comparable with those obtained in rat and monkey malaria. He suggests that his results indicate that the nutritional deficiencies induced by a milk diet do not affect the multiplication of *P. falciparum* and *P. malariae*. This may indicate that different species of malaria parasites may have differing nutritional requirements, or that the human host may be more efficient in supplying vital nutrients to the parasite. He admits the possibility that the powdered milk used in these experiments may have contained sufficient *p*-aminobenzoic acid and other essential substances to negative the inhibitory effect of milk.

B. G. Maegraith

Delannoy, A. & Hugon, J. Essai de prophylaxie antipaludique en milieu rural au moyen de pyriméthamine (Daraprim). [**Trials of Prophylaxis of Malaria with Pyrimethamine in a Rural Area in the Belgian Congo**] *Ann. Soc. Belge de Méd. Trop.* 1954, Aug. 31, v. 34, No. 4, 397–405.

The investigations here recorded were carried out in 3 villages situated in a highly malarious area about 120 miles south-east of Léopoldville, in the Belgian Congo, over a period of 6 months.

Daraprim (pyrimethamine) was administered to children up to 15 years of age; it was given in a dosage of 12·5 mgm. to those from 0 to 5 years and 25 mgm. to those from 5 to 15. In two of the villages (A and B) the drug was given once a month; in the third village (C) it was given fortnightly. Altogether 134 children were treated, 58 in A and B, and 76 in C.

The parasite rate [*P. falciparum*] in A and B was 62 per cent. immediately before drug administration was begun; in C it was 65·6 per cent. After 3 months it had fallen to 10·3 per cent. in A and B and to 3·9 per cent. in C. After 6 months, blood films taken from all the children were negative, except one in village C. Spleen rates among children in the 3 villages fell during the 6 months from 67·2 to 5·7 per cent. There was no evidence of toxicity in any of the children treated.

It is concluded that pyrimethamine is a particularly suitable drug for the control of malaria among the child population of an endemic area, and that a monthly dosage of 12·5 mgm. for children from 0 to 5 years of age and 25 mgm. for those from 5 to 15 years is sufficient for effective protection.

G. Covell

Chaudhuri, R. N. & Chakravarty, N. K. **Pyrimethamine in the Prophylaxis of Malaria.** [Memoranda.] *Brit. Med. J.* 1955, Jan. 22, 207.

The work here recorded was carried out in a malarious village situated 35 miles from Calcutta during the period July to December, when transmission is usually most active.

Alternate classes in the village school received a weekly dose of pyrimethamine (172 boys) or dummy tablets (139 boys) respectively, the dose of pyrimethamine given being 12·5 mgm. to those under 10 years of age and 25 mgm. to those aged 10 years and upwards. A preliminary survey showed that 60 per cent. of malarial infection in the area was due to *Plasmodium falciparum* and 40 per cent. to *P. vivax* or *P. malariae*.

During the period of drug administration the parasite rate in the treated group fell from 5·7 per cent. in July to 0·7 per cent. in November. The figure rose again to 2·3 per cent. in December, some weeks after drug distribution had been discontinued. In the group which received no antimalarial drug the parasite rate rose from 3·6 in July to 6·6 in November and 9·2 in December. The incidence of overt malaria in the 2 groups could not be accurately determined, but from enquiries made at the weekly visits it was learned that febrile attacks were much less frequent in the treated group.

It was concluded that pyrimethamine administered at weekly intervals in the dosage used is an effective suppressant of malaria. The persistence of *P. falciparum* parasites in a few children during administration of the drug was attributed to the presence in the area of strains of this species of parasite relatively less sensitive to the drug. *G. Covell*

Portman, R. F. **Control of Mosquitoes in California Rice Fields.** *J. Econom. Entom.* 1954, Oct., v. 47, No. 5, 818–24. [17 refs.]

In the past 10 years the acreage of rice grown in California has doubled, amounting to 412,000 acres in 1953, and it has been increasingly necessary to improve measures for controlling *Aëdes dorsalis* and *Aëdes nigromaculis*, biting pests, and *Culex tarsalis* and *Anopheles freeborni* which are, in addition, vectors respectively of encephalitis and malaria; there were 804 human cases of encephalitis in 1952, mainly from the rice-field areas.

Breeding of *Aëdes dorsalis* (and *Aëdes nigromaculis*), the eggs of which are dormant in the mud preceding the flooding of the rice fields, is now controlled mainly by mixing 50 per cent. DDT wettable powder with rice seed which is sown from aircraft, giving 0·25 to 0·5 lb. DDT per acre. Spraying of DDT at 1 lb. per acre before flooding is also very effective. The DDT is a useful control, moreover, of crustacean and water beetle pests of rice.

Measures against *A. freeborni* are applicable also to *C. tarsalis*. Overwintering adults are controlled by indoor aerosols from ground equipment, with 5–10 per cent. DDT formulations. *C. tarsalis* is now considered to be showing DDT-resistance in some areas and BHC and other insecticides are in use. Two per cent. thiocyanate (Lethane 384) is sometimes included to stimulate the mosquitoes from less accessible recesses and improve the kill. Indoor residual spraying with DDT as practised widely in malaria control is also used and is more effective than aerosols. It is important to control early breeding of these mosquitoes in spring in ditches, borrow pits, etc. to reduce subsequent invasion of the extensive flooded rice-fields later in the year; accessible rice-fields are controlled during the summer but much of the flooded area cannot be dealt with easily. Recourse has been made to outdoor aerosol dispersions from aircraft against adults, but

this is possible only on infrequent occasions when the weather is suitable. On the other hand, spraying a mixture (0·024 lb. dieldrin per gallon and 2 per cent. Lethane) from aircraft at 4 gallons per acre is more practicable and very effective for adults, besides larvae, under less exacting weather requirements. An important practical development is plane-spraying 10 days before the rice-fields are drained in the autumn to check breeding in the pools and the like as the fields dry off before cropping.

Although these measures, applied at times and conditions varying from year to year according to weather and from district to district in a single season, have greatly reduced mosquitoes there still remains sufficient breeding to maintain a risk of malaria transmission and, particularly, of encephalitis since *C. tarsalis* appears to be increasing, and to be resistant to some of the insecticides. *D. S. Bertram*

Giglioli, G. **Residual Effect of DDT in a Controlled Area of British Guiana tested by the Continued Release of *Anopheles darlingi* and *Aedes aegypti*: a Practical Technique for the Standardized Evaluation of Over-All Residual Efficiency under Field Conditions.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1954, Nov., v. 48, No. 6, 506–21, 3 figs.

Anopheles darlingi and malaria were eradicated from a large part of British Guiana by a residual insecticide programme, which in the locality of Mon Repos started in February 1945 with one application of 100 mgm. DDT per square foot and was followed by 5 others of 150 mgm. at intervals of 10, 8, 9, 9 and 10 months, the last being in February 1949. The houses here, though undoubtedly extreme slums, are almost uniquely suitable for the long maintenance of residual activity; in particular they have hard wood walls and are rarely cleaned. In order to test the duration of subsequent lethal action large numbers of mosquitoes were liberated in a typical area between August 1949 and July 1952. About 95,000 *A. darlingi* were introduced as larvae and pupae but intensive searching failed to reveal a single surviving specimen or a single breeding focus derived from them. Equally no surviving adults were found from about 150,000 *Aëdes aegypti* introduced as larvae or pupae. However, in the course of these searches 4 *A. aquasalis* were found and 576 *Culex fatigans*, while *A. aquasalis, A. albitarsis* and *A. triannulatus* were found breeding, the first two freely. *A. darlingi* previously bred very freely in this area.

The mosquitoes in these tests were allowed to emerge in the open air near the houses. Parallel tests with larvae in bowls in the houses from 1950 to 1952 showed that no adults hatched from 324 *A. darlingi* larvae introduced, and 1 only of 434 *Aëdes aegypti* larvae, though hatching took place freely in bowls protected from dust. It is concluded that in these houses a lethal concentration of DDT dust is maintained for very long periods. It was, however, shown that this conclusion does not apply to new cottages which are well ventilated and lighted and which are more consistently cleaned by the occupants.

The dose and cycle of insecticide are usually chosen empirically and may result in great wastage. No general prescription can be made but biological testing following this pattern can determine a proper combination for any area. It is suggested that *Aëdes aegypti* should be used as a test insect, its comparative susceptibility in relation to the malaria vector being previously determined in the laboratory. A technique for such experiments is proposed and local evidence is brought to show that the consequent temporary infestation with *Aëdes aegypti* can be rapidly terminated.

G. Macdonald

Nair, C. P. **Animals in Malaria Research.** *Bull. Nat. Soc. India for Malaria & other Mosquito-Borne Dis.* 1954, Nov., v. 2, No. 6, 200–207. [Numerous refs.]

A brief account is given of the use of animals in malaria research, starting with the discovery of malaria parasites in birds by Danilewsky and of their transmission by mosquitoes by Ross, and continuing up to the present day with the isolation of *Plasmodium berghei* in rodents. Fundamental knowledge regarding the life cycle of the parasite has been acquired by observations on the infections in birds and monkeys, and the immunological response has also been intensively studied in these animals. The chemotherapy of malaria owes much to work on birds and monkeys, and more recently on rodents. A direct practical amplification of animal malaria lies in the interpretation of sporozoite rates, as the parasites may be non-human in places where animal infections are common.

P. C. C. Garnham

Ray, A. P. **Role of Blood Transfusion in Liver Injury due to** *P. knowlesi* **Infection in Monkeys.** [Research Notes.] *Bull. Nat. Soc. India for Malaria & other Mosquito-Borne Dis.* 1954, Nov., v. 2, No. 6, 213–14.

The marked effect of blood transfusions in preventing liver damage in Rhesus monkeys infected with *Plasmodium knowlesi* was clearly demonstrated. Nine monkeys with a parasitaemia of 40 per cent. were divided into groups of three: (1) received transfusions of whole blood and a single dose of chloroquine, (2) received plasma and chloroquine, and (3) received chloroquine alone. Monkeys in the last two groups all died in the usual way; in the first they all recovered and biopsies of liver carried out 1, 2, 4 and 7 days after clearance of parasites showed a rapid disappearance of the fatty changes in the parenchyma cells. Centrilobular necrosis and widespread fatty degeneration were present in the livers of the 6 monkeys which died. The important suggestion is made that blood transfusions might be used with advantage in severe cases of *P. falciparum* malaria in man.

P. C. C. Garnham

Fabiani, G. & Orfila, J. Action du régime lacté sur le paludisme expérimental de la souris blanche. [**Effect of Milk Diet on Experimental Malaria in Mice**] *C.R. Soc. Biol.* 1954, July, v. 148, Nos. 13/14, 1239–41.

Thirty-two adult white mice were placed on a milk diet (fresh cow's milk or condensed "Gloria" milk) 3–5 days before being inoculated with *Plasmodium berghei* (in amounts varying between 100,000 and 50,000,000 parasites), and the course of the infection was studied. The animals responded in 5 ways: (1) 12 mice showed a low parasitaemia (with few reticulocytes) for 10 days, followed by a progressive rise, ending in death of the animals about the 20th day; (2) 8 mice showed irregular fluctuations in parasitaemia; (3) 3 mice showed a parasitaemia not amounting to more than 4 or 5 per cent., but death occurred in a week; (4) 5 mice showed a low irregular parasitaemia, and (5) 4 mice behaved like (4) above, but parasites eventually disappeared, although reticulocytes persisted in large numbers. In two mice the disappearance of the infection was permanent; they were re-inoculated with large numbers of parasites and were returned to a normal diet, when only a slight infection developed, which soon ended. A state of immunity had therefore developed. The effect of a milk diet on

P. berghei infections in mice is thus seen to be highly variable and acting either on the blood and blood-forming elements, or perhaps directly on the parasite itself.
P. C. C. Garnham

Fulton, J. D. **Cortisone and *Plasmodium berghei* Infection in Rodents.** *Ann. Trop. Med. & Parasit.* 1954, Sept., v. 48, No. 3, 314–17, 1 graph.

Rats (weighing 180 gm.) and mice (20 gm.) were infected with *Plasmodium berghei* and subsequently received up to 90 mgm. (proportionately less for mice) of cortisone acetate during 5 days. The animals were fed on a cube diet or on milk supplemented with vitamins. No increase in parasitaemia was observed in cortisone-treated animals as compared with a control group, with the exception of one rat on a cube diet which suffered from a very heavy infection for 18 days. The course of infection in mice was totally uninfluenced by the drug. In both rats and mice, cortisone had a profoundly toxic action, killing them in 16 days or less. [See also Schneider, this *Bulletin*, 1954, v. 51, 764, and Roberts, *ibid.*, 885; 1955, v. 52, 253.]
P. C. C. Garnham

Galliard, H., Lapierre, J. & Golvan, Y. L'hyaluronidase dans les infections à protistes sanguicoles et en particulier *Plasmodium berghei*. Action comparée avec la phénylhydrazine. Rôle et signification de la réticulocytose. [**Hyaluronidase in Protozoal Blood Infections, especially *Plasmodium berghei*. Comparison with Phenylhydrazine. The Part played by Reticulocytes**] *Ann. Parasit. Humaine et Comparée*. 1954, v. 29, No. 4, 330–46, 8 figs. [12 refs.]

A diffusion factor, of enzymic nature, named hyaluronidase has been known for about a quarter of a century, and was first isolated from testicular tissue. Similar enzyme factors have been described from other sources including bacteria, protozoa and worms [this *Bulletin*, 1953, v. 50, 223, 1138; 1954, v. 51, 408, 435]. Through the action of this factor on hyaluronic acid which is one of the components of connective tissue, substances introduced subcutaneously, whether liquid or particulate in character, may spread more rapidly.

The authors have previously noted the effects of hyaluronidase on infection with *P. berghei* in rats and mice, and in the latter it generally gave rise to reduced prepatent period and increase in the peak of parasitaemia. More extended experiments have substantiated earier observations. Thus the effect of hyaluronidase given during infection with *P. berghei* in mice is very small, whereas in young rats the prepatent period is reduced and death occurs earlier owing to heavier parasitaemia. The rat, normally refractory to subcutaneous inoculation with *P. berghei*, develops a virulent infection after administration of hyaluronidase. The final result of the enzyme action, which functioned by aiding diffusion and did not affect the blood picture, resembled that of phenylhydrazine, which markedly affects reticulocytosis. The action of B12 resembled that of phenylhydrazine.

The effect of hyaluronidase was tried in a number of trypanosome infections, also in infection due to *Babesia rodhaini*, *P. vinckei*, *Spirochaeta hispanica* and *Toxoplasma* without any notable effects being observed, but a marked increase in the severity of infection with *P. gallinaceum* resulted.
J. D. Fulton

Fabiani, G. & Orfila, J. Action d'un traitement sulfamidé sur le paludisme expérimental de la souris blanche. [**Action of Sulphonamide Treatment on Experimental Malaria in the White Mouse**] *C.R. Soc. Biol.* 1954. Aug.–Sept., v. 148, Nos. 15, 16, 17 & 18, 1390–92.

The efficacy of sulphonamides in treatment of *P. berghei* infections in mice reported earlier [this *Bulletin*, 1950, v. 47, 1183; 1951, v. 48, 130] has been confirmed. A more detailed investigation of the nature of the response to these drugs and of the immunity following such treatment has now been made. One strain of parasite was maintained in mice on normal diet and another in mice on milk diet for long periods. The drug, Soludiazine, was given in 5 daily doses of 0·1 mgm. subcutaneously starting about a week after inoculation. The conclusions reached by the authors were that the effect of the drug depends on the individual host, on the presence or absence of the spleen, and on the strain of parasite used. The sulphonamide was particularly effective against a strain of parasite maintained in hosts on milk diet. As a result of the drug treatment the host was able to develop an immunity to this otherwise lethal infection as shown by the usual tests. *J. D. Fulton*

Rodhain, J. Absence d'immunité croisée entre *Plasmodium berghei* et *Plasmodium vinckei* dans les infections chez les jeunes rats. [**Absence of Cross Immunty between** *Plasmodium berghei* **and** *Plasmodium vinckei* **in Infections in Young Rats**] *C.R. Soc. Biol.* 1954, Aug.–Sept., v. 148, Nos. 15, 16, 17 & 18, 1519–20.

The author has again demonstrated an antigenic difference between the two rodent parasites *Plasmodium berghei* and *P. vinckei* [this *Bulletin*, 1953, v. 50, 913; 1955, v. 52, 128], by inoculating animals with *P. vinckei* after cure of infection with *P. berghei*. Two rats of 120 gm. weight, which had recovered from a *P. berghei* infection, were inoculated with *P. vinckei*; the blood of both showed parasites for 7 and 11 days respectively. A second experiment employed 4 rats weighing between 35 and 50 gm. These were inoculated with another strain of *P. berghei*, from which infection they recovered in 15 to 22 days. They were then given *P. vinckei* and all became infected with this parasite which persisted in their blood for 10 to 27 days and showed the typical morphological features. Subinoculations into mice confirmed that the parasite was *P. vinckei* and not a relapse of the earlier *P. berghei* infection. The course of the *P. vinckei* attacks in both experiments resembled the normal course of the disease, and the absence of cross immunity is thus clearly shown. *P. C. C. Garnham*

Trembley, Helen L. & Greenberg, J. **Further Studies on the Hybridization of Strains of** *Plasmodium gallinaceum*. *J. Parasitology*. 1954, Aug., v. 40, No. 4, 475–9. [11 refs.]

The authors had previously shown [see this *Bulletin*, 1954, v. 51, 1227] that inoculation of mixed strains of *Plasmodium gallinaceum* into chicks produced infections which after the first mosquito passage (F_1) exhibited some of the characters of both strains, but after a second passage (F_2), the infection apparently belonged to one type only. In these new experiments, the F_1 mixture or hybrid was exposed on the ninth day to a single dose of pyrimethamine (Daraprim) in order to facilitate further hybridization, if such a process occurred; some chicks died of an exo-erythrocytic infection

before or soon after treatment, of the remainder, several showed rare tissue forms in brain smears 15 to 17 days after the drug was given. On these survivors mosquitoes were fed and infections produced by their sporozoites were accompanied by no exo-erythrocytic forms. A possible explanation for these results is said to lie in the combination of one strain carrying a cytoplasmically-inherited factor and the disproportion of gametocyte production.

P. C. C. Garnham

TRYPANOSOMIASIS

In this section abstracts are arranged as far as possible in the following order:—African—*human, animal;* American—*Chagas's disease and other trypanosome infections. In each form the following order is followed*:—*epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control.*

Nigeria, Northern. **Sleeping Sickness Service (Northern Nigeria) Annual Report. April 1953–March 1954.** 7 mimeographed pp. [1954.]

During the year under review the sleeping sickness service was incorporated into the Regional Medical Headquarters. Some matters of general interest are worthy of comment. Owing to the low incidence of human trypanosomiasis in recent years in Northern Nigeria, native administrations and the population generally have lost their fear of it and it is becoming increasingly difficult to obtain their full cooperation in re-surveys. The risk of recurrence still exists as indicated by the recent discovery of a focus in Kano Province. The continuous rise in the relapse rate over the last 7 years from 11·5 to 26·3 per cent., suggests that chronic sleeping sickness is likely to become a major problem and for this reason intensive field studies of the new trypanocidal drugs are being carried out. The control of tsetse infestation of mango groves has been attempted by pruning all branches up to 6 feet from the ground or by spraying with DDT; both methods have given satisfactory results. Details of the activities of the service in the various affected areas are recorded in tables, which indicate that control is being maintained and improved, though Benue Province continues to provide a high proportion of cases of sleeping sickness, some 40 per cent. of the 6,613 diagnosed during the year.

T. H. Davey

Harley, J. M. B. **The Breeding Sites of the Tsetse Fly** *Glossina morsitans*. *Acta Tropica*. Basle. 1954, v. 11, No. 4, 379–402, 20 figs.

Glossina morsitans from the north-central fly belt of Tanganyika are generally paler than those from the western belt [this *Bulletin*, 1951, v. 48, 133]. The author studied the distribution of pupal sites in different seasons of the year for both forms in, respectively, Singida district and Kahama district; seasonal shift of preferred sites for pupae was investigated. Climatic, soil and vegetational features of the two districts are described and followed by an account of the findings illustrated by 20 excellent photographs of pupal sites. In both areas logs were the most important type of site. In Singida, but not in Kahama, it was observed that the size of the logs used for shade doubled in the hot season and only in this season were

rot holes, thickets and leaning trees also in use; and these were shown to be the most shaded and coolest places available. Such sites occurred, in the hot season, in valleys which were generally more shady than the leafless woodland. In cool, wet seasons long grass in these valleys did not serve for pupae, which were to be found back in the now leafy woodland. In Kahama, pupae were present in the woodland throughout the year and, perhaps because in the year of observation long grass persisted in the valleys, pupal sites were not usual in them.

Neither light nor saturation deficiency at the sites appeared to be factors controlling choice by the female flies, but there was evidence that soil temperature at 1½ in. depth was of some importance, although alone not necessarily a good index. The range over the seasons varied from 21·4°C. to 27·7°C. A general conclusion is that although tsetse find cooler sites in the hot season and rather warmer sites in the cool season for their pupae, the temperature control obtained is not precise but lies within an average range as great as 4°C.

D. S. Bertram

Jackson, C. H. N. **The Hunger-Cycles of *Glossina morsitans* Westwood and *G. swynnertoni* Austen.** *J. Animal Ecology.* 1954, Nov., v. 23, No. 2, 368–72, 1 fig.

Glossina morsitans in East Africa typically occurs in woodland of broad-leaved trees (*Brachystegia*, etc.) which has a good, high canopy in the rainy season and still provides some shade in the leafless dry season. *G. swynnertoni*, on the other hand, more restricted in its range in northern Tanganyika and southern Kenya, is associated with a more xerophytic, sparser vegetation of thorny *Acacia* and *Commiphora* spp. interspersed with small thickets (*Grewia*, etc.) where overhead shade is very limited. Laboratory observations on the survival of these two species in identical conditions (25°C. and 50 per cent. relative humidity) failed to indicate that *G. swynnertoni* was more adapted to resist desiccation than *G. morsitans*. Since relative amounts of fat and non-fatty solids (the latter probably undigested blood constituents) in the two species showed a higher level of the supposed blood constituents in *G. swynnertoni* it was thought that this species met the risk of desiccation by more frequent blood meals.

This paper reports on field experiments in a *G. morsitans* area (Kakoma) and a *G. swynnertoni* area (Shinyanga) to test this point. The Shinyanga area was shown to be more arid than Kakoma, as seemed apparent from the vegetational characteristics. Statistical treatment of data on weights of marked wild-caught flies and on subsequent recapture of them in these areas revealed that *G. swynnertoni* is able to live in the arid bush of its Shinyanga environment by feeding every 2½ or 3 days; host animals are in general quite numerous. *G. morsitans* feeds every 3 or 4 days and although able to extract more reserve nourishment from the less frequent meals it also requires the protection of a well-shaded environment.

These observations refer to the mid-dry season (September and October). The hunger cycle is probably twice as long at the end of the rains.

D. S. Bertram

Janssen, P. Le test de Thorn dans la maladie du sommeil. [**The Thorn Test in Sleeping Sickness**] *Ann. Soc. Belge de Méd. Trop.* 1954, Aug. 31, v. 34, No. 4, 453–62.

Thorn's test affords information on the activity of the hypophyseal and suprarenal cortex systems. The test is done by injecting 0·3 mgm. of

adrenaline subcutaneously, or 25 mgm. of corticotrophin intramuscularly, and determining the number of circulating eosinophils before and after the injection. When the test is normal there is a maximum fall in the number of circulating eosinophils about 4 hours after the injection, and the fall exceeds 50 per cent. The adrenaline test should be done first; if it gives a normal response this shows that both glandular systems are functioning normally. If, however, the fall in the eosinophil count after adrenaline is less than 50 per cent. (and so the test is abnormal), a corticotrophin test should be done; if this also fails to produce a 50 per cent. fall in the number of eosinophils it shows that the suprarenal function is abnormal. But if, though the adrenaline test is abnormal, the corticotrophin test causes a normal fall of over 50 per cent. in the eosinophils the conclusion is that the hypophyseal function is abnormal. Actual details of the preparation of the patient and of the performance of the tests are given in the text.

Twenty patients at Usumbura in Ruanda-Urundi province, who had unsuccessfully been treated for late-stage trypanosomiasis by repeated tryparsamide treatments, and in all of whose cerebrospinal fluids trypanosomes had been found, were subjected to these tests. The details and data are set out in a table. Of 19 given the adrenaline test 11 gave a normal response; of the 8 who did not do so, with the corticotrophin test 3 gave evidence of suprarenal and 5 of hypophyseal inadequacy. On the twentieth case no adrenaline test was done, but a corticotrophin test showed a suprarenal defect.

The interpretation of the Thorn test is open to error in several conditions, which include eosinopenia, refractory eosinophilia, low basal metabolism, atrophy or hypofunction of the suprarenal cortex due to chronic hypophyseal insufficiency, and an abnormal rate of fall in the eosinophil count; examples of the results of the test in such conditions are given.

On the author's findings Thorn's test affords some information of interest in the investigation of late-stage trypanosomiasis, and it might assist in the interpretation of the pathology of this condition. *A. R. D. Adams*

McLetchie, J. L. & Duggan, A. J. **A Note on Trypanosomiasis.** *West African Med. J.* 1954, Dec., v. 3 (n.s.), No. 4, 172–9, 1 fig.

The word *kpatsungi* is applied among the Nupe and some other peoples of Nigeria to a condition in which the cervical glands are enlarged. The authors have studied the etymology and usage of this word among the Nupe and the Yagba peoples. Sleeping sickness is a cause of enlargement of glands in the neck, and so this disease is readily confused with *kpatsungi*. There is an interesting account of the native methods of treatment of *kpatsungi*; among these multiple incision is popular, though it is not so popular as it once was in those areas where the presence of sleeping sickness is now fully appreciated. A case of *kpatsungi* and trypanosomiasis, so treated, was seen by the authors after the cerebrospinal fluid had undergone the classical changes of sleeping sickness and contained trypanosomes.

A. R. D. Adams

Michielsen, P. & Triest, A. Action toxique de l'Arsobal sur le système cardiovasculaire. [**Toxic Action of Arsobal on the Cardiovascular System**] *Ann. Soc. Belge de Méd. Trop.* 1954, Aug. 31. v. 34, No. 4, 485–90, 3 pls.

Arsobal, or 3854 RP, is extremely valuable in the treatment of trypanosomal infections which have become refractory to other drugs.

Unfortunately it is toxic and may cause such conditions as arsenical encephalopathy and albuminuria. The present authors have found myocardial damage and a rise in blood pressure to result from the use of the drug in 5 of 6 consecutive patients treated with it. Details are given of these cases and their investigation and treatment, and attached are some ECG recordings. A summary of information culled from the literature on the toxic effects of arsenicals and of BAL on the cardiovascular system indicates that both may produce myocardial changes; and hypotension, and more commonly hypertension, have been ascribed to the intravenous injection of BAL, though these have been of brief duration.

While recognizing the danger of drawing firm conclusions from so few cases over an observation period of only 3 months, the authors believe that the changes in the cardiovascular systems of their patients after Arsobal treatment are sufficiently marked to justify the warning that this drug should be used only in trypanosomiasis patients in whom other drugs are ineffective. *A. R. D. Adams*

Hocking, K. S., Yeo, D. & Anstey, D. G. **Aircraft Applications of Insecticides in East Africa. VI.—Applications of a Coarse Aerosol containing DDT to control the Tsetse Flies,** *Glossina morsitans* **Westw.,** *Glossina swynnertoni* **Aust. and** *Glossina pallidipes* **Aust.** *Bull. Entom. Res.* 1954, Sept., v. 45, Pt. 3, 585–603, 2 figs.

This paper, and the two following, record further experiments in this series [see this *Bulletin*, 1954, v. 51, 31, 32, 472, 473, 855]. A further trial of air spraying was conducted in the Kikore district in Tanganyika which had been the site of earlier tests described by Hocking *et al.* [*ibid.*, 473]; the unsprayed block [Galapo block] formerly used as a control was treated. This block of woodland is roughly rectangular, measuring about 2 miles by 7. A fairly detailed description of the flora and fauna is given. Briefly, the vegetation at the western end is more profuse and massive, with a canopy at 60 to 70 ft. In the centre is a large circle of open grassland with few trees; the eastern end consists of dry thickets and thorn bush. A considerable amount of game visited the area and some lived permanently in the block.

Three species of tsetse infested the area: *G. morsitans* and *G. pallidipes* being largely confined to the western part of the block, whereas *G. swynnertoni* was found in greater numbers in the eastern half. *G. morsitans* was caught in greatest numbers and by releasing marked flies it was estimated that about 10,000 non-teneral males of this species were present originally. The block was well isolated from other tsetse-infested areas by clearings of at least 1½ miles.

The air spray treatment was done by two Avro Anson aircraft from a locally prepared air strip (which cost only £30). These machines were fitted with 52 ft. spray booms on which 24 Bray nozzles were mounted. The insecticide was 10 per cent. technical DDT dissolved in Diesolene, of which the aircraft carried 110 to 130 gallons. The spray liquid was pumped to the nozzles by a pump driven by a small airscrew, giving a pressure of 150 lb. per sq. in. This gave an output of 8–10 gall. per minute; and flying at about 100 m.p.h. with a 55 yd. wide swathe gave a nominal dosage of 0·25 gall. per acre (0·25 lb. DDT). In the whole trial, the block was treated 7 times over a period of 15 weeks (at least 2 and possibly 3 pupal periods). Each treatment required 9 to 11 sorties which were planned to overlap the previously treated area by 500 to 600 yards. Attempts were made to ascertain the drop-size spectrum which appeared

to be rather better than before; the mass mean diameter was about 60 microns.

The effects on the tsetse were judged by fly rounds on 7 pre-determined paths, before and at regular intervals after treatment. As in the previous trials, a very great reduction of tsetse was obtained, which persisted for at least 18 months after the end of the treatments. The effect was most pronounced with *G. pallidipes*, which virtually disappeared, and appears to have been eradicated from the block. The reduction of *G. morsitans* was about 98 per cent. and that of *G. swynnertoni* about 94 per cent. The differences in these results are discussed in some detail, with reference to the data from different parts of the block. It is not unlikely that there are inherent differences in susceptibility between the various species.

This trial was not quite so successful as were the best results obtained in earlier work, possibly because the air spray was hampered in the later stages by development of leaves on the trees, which had been bare throughout the previous tests. Nevertheless, it has substantiated the previous finding that tsetse populations in isolated bush can be greatly reduced by air spraying of insecticide and that they remain low for a long time afterwards. This may be of value in the initial stages of re-settlement schemes. The cost is high (about £1,000 per sq. mile) most of it being due to the standing charge on the aircraft (£11,000 per annum) which is much more than the actual operating costs. It is more expensive than discriminative clearing or the killing of game, but compares favourably with sheer clearing of bush. The latter method is, of course, a certain way of eliminating tsetse. *J. R. Busvine*

Hocking, K. S., Burnett, G. F. & Sell, R. C. **Aircraft Applications of Insecticides in East Africa. VII.—An Experiment against the Tsetse Flies, *Glossina morsitans*, Westw. and *G. swynnertoni* Aust., in the Rainy Season.** *Bull. Entom. Res.* 1954, Sept., v. 45, Pt. 3, 605–12, 2 figs. on pl.

This trial was conducted on the site of previous experiments, like the work described in the paper above. The area used was a block of woodland, described in earlier work as the "North Block". It had been air-sprayed with DDT in 1949, with the result that its tsetse population was much reduced and continued low for two years afterwards. (Just before the trial described in this paper, the numbers of *G. morsitans* were only about 4 per cent. of the numbers before the 1949 test and those of *G. swynnertoni* about 10 per cent.)

The present trial extended from January to May 1951, during the wet season. This was unfavourable in several ways. The aircraft could not use the air strip near the site and had to fly from Arusha, thus losing some of the short time daily available for effective air-spray. On several days flying had to be completely cancelled owing to bad conditions. The roads became impassable to motors, which hampered the ground markers for directing the spraying runs of the aircraft. Finally, the trees in the woodland were in full leaf, which must have blanketed much of the spray.

The insecticide used in the trial was *gamma* BHC. Owing to the difficult conditions, it was used at high concentrations, with as wide a swathe width as possible. The spray fluid was 20 per cent. BHC, equivalent to 2·45 per cent. *gamma* isomer, applied in 75-yard swathes to give a nominal dosage of 2·42 lb. technical BHC per acre. The method of application was as in the previous paper (but with fewer nozzles on the boom)

and the drop spectrum was similar. Seven complete and one partial treatment were made.

Estimations of entomological results were made by fly rounds on predetermined paths, as usual. The data were corrected (by Abbott's formula) for a decline in numbers of tsetse observed in a control area. With this adjustment, the effect of the treatment was to reduce the population of *G. morsitans* by 80 per cent. and that of *G. swynnertoni* by 64 per cent. The final figures were, of course, very low, but there was no suggestion of complete eradication. The numbers of tsetse remained somewhat below the early 1950 figure for some 18 months after the trial. *J. R. Busvine*

Hocking, K. S., Burnett, G. F. & Sell, R. C. **Aircraft Applications of Insecticides in East Africa. VIII.—An Experiment against the Tsetse Fly, *Glossina swynnertoni* Aust., in an Isolated Area of Thornbush and Thicket.** *Bull. Entom. Res.* 1954, Sept., v. 45, Pt. 3, 613–22. 1 text fig. & 2 figs. on pl.

This paper records another experimental air-spraying of a block of tsetse infested bush, near Kikore in the Central District of Tanganyika. The area is known as the "Atta" block and is about 2 miles south of the "South Block" mentioned in a previous paper by Hocking *et al.* [this *Bulletin*, 1954, v. 51, 473]. This woodland had been previously isolated from other tsetse-infested zones for a trial of *gamma* BHC smoke generators (unpublished), and the minimum clearing was of $1\frac{1}{2}$ miles. The block is a well-marked area of thorn bush and thicket, about $3\frac{1}{2} \times 1\frac{1}{4}$ miles in extent. *G. morsitans* was found only in very small numbers at any time. The numbers of *G. swynnertoni* had been drastically reduced by the smoke generator trial, but thereafter increased to a low level and remained stationary (in the region of 70 non-teneral males per sq. mile) for a year before the trial started.

The treatments covered the period November 1951 to February 1952, during the rainy season. Conditions were bad, as in the second trial on the North Block [see above]; many flights were necessarily from Arusha and several were cancelled, so that the treatments were delayed. In all, 5 complete and 3 partial treatments were given.

The insecticide used was 10 per cent. technical DDT in Diesolene applied at a nominal rate of 0·25 gallons per acre in 88-yard swathes. The equipment and methods were substantially the same as in the second North Block trial.

The entomological results depending on the usual fly rounds were compared with similar data from the old South Block which was used as a control. The *G. swynnertoni* was reduced from an apparent density of about 7 to zero after the second application and no flies were caught for 6 months after the 5th treatment. A few were caught at intervals after this, but there is a possibility that they may have been immigrants following vehicles or men and cattle. In any case the experiment was much more successful than the Galapo Block trial in the same area [see Hocking, Yeo and Anstey, above, p. 344]. Various factors are compared in these trials and it is concluded that the only valid difference was the initially smaller tsetse population at Atta. If this was reduced to the same proportionate extent, it might have more difficulty in re-establishing itself. The poorer results in the first North Block trial as compared to those obtained in the Atta block trial may have been due to immigration of flies in the former site. *J. R. Busvine*

Yeo, D. **Aircraft Applications of Insecticides in East Africa. IX.—Further Experiments on the Deposition in Open Country of a Coarse Aerosol released from an Aircraft.** *Bull. Entom. Res.* 1954, Dec., v. 45, Pt. 4, 745–9, 3 figs.

In an earlier paper [this *Bulletin*, 1954, v. 51, 855] Yeo and his colleagues investigated the effects of atmospheric conditions on the ground deposits of coarse aerosol emitted by aircraft. Further trials were done with the same technique. Atmospheric turbulence was again measured by the factor F, which depends upon temperature, lapse rate and wind speed. In the earlier tests the aircraft flew at 30 ft. and, in these experiments, at 65 ft.

The results were not greatly different. Ground deposits were greater under calm conditions (particularly near the track of the aircraft), the total deposit being strongly correlated with F. As might be expected, the deposit was somewhat slower in forming; but after 30 seconds the rate of deposition began to rise rapidly. It appears that after about 150 to 200 seconds the final deposits from aircraft at 30 and 65 ft. would be the same under similar atmospheric conditions. *J. R. Busvine*

See also p. 412, Lewis, **Studies concerning the Uptake of Contact Insecticides. I.—The Anatomy of the Tarsi of certain Diptera of Medical Importance.**

Agosin, M. & von Brand, T. **Studies on the Carbohydrate Metabolism of *Trypanosoma congolense*.** *Exper. Parasit.* New York. 1954, Nov., v. 3, No. 6, 517–24. [24 refs.]

"1. The rate of oxygen consumption of *T. congolense* is nearly as high as that of the trypanosomes of the evansi-brucei groups, but its rate of glucose consumption is lower.

"2. The *R.Q.* is high.

"3. The main metabolic end products, accounting nearly quantitatively for the degraded glucose, are acetic acid, pyruvic acid, and carbon dioxide. Succinic acid was produced at most in traces, no lactic, citric, malic, formic, propionic or higher volatile acids were excreted, nor was ethyl alcohol formed."

See also p. 339, Galliard *et al.*, L'hyaluronidase dans les infections à protistes sanguicoles et en particulier *Plasmodium berghei*. Action comparée avec la phénylhydrazine. Rôle et signification de la réticulocytose. [**Hyaluronidase in Protozoal Blood Infections, especially *Plasmodium berghei*. Comparison with Phenylhydrazine. The Part played by Reticulocytes**]

Pizzi, T., Rubio, Mafalda & Knierim, Feliza. Inmunología de la enfermedad de Chagas. [**The Immunology of Chagas's Disease**] *Bol. Chileno de Parasit.* 1954, Apr.–June, v. 9, No. 2, 35–47, 2 graphs. [46 refs.] English summary.

In this paper the authors give a summary account of investigations on the immunology of Chagas's disease in the course of the preceding 5 years, details of which were published in a number of previous papers from the Parasitological Department of the University of Chile. In the past, work

on this subject was hampered by the absence (a) of strains of *Trypanosoma cruzi* of uniform virulence, (b) of quantitative methods for assessing the results of experiments, and (c) of a technique for immunizing animals. The first difficulty was overcome by using for the experiments (a) inbred homozygous strains of mice (C3H) and rats (A-C), and (b) a highly virulent Chilean strain of *T. cruzi* ("Telahuén"), which, when inoculated in a dose of 100,000 parasites, regularly produces in C3H mice a progressively increasing parasitaemia reaching a density of 5,000 trypanosomes per cmm. of blood, with a special predilection for cells of the connective tissue, and killing the animals in 10–12 days. For the enumeration of the trypanosomes in fresh blood, specially graduated pipettes and square-ruled coverslips were used. Finally, immunization was carried out by two methods: (a) with heavy doses of cultures of *T. cruzi* in Senekjie's medium [this *Bulletin*, 1944, v. 41, 548], previously attenuated by numerous (250–300) passages, and (b) with virulent blood trypanosomes accompanied by simultaneous administration of primaquine.

In experiments conducted by these methods, it was demonstrated that the C3H mice are only slightly resistant to a virulent strain of *T. cruzi*, which multiply in the fibroblasts, fixed macrophages and muscle fibres. At the sites of infection there is an inflammatory reaction, with phagocytosis of the parasites by macrophages in the inflammatory nodules. Though this is regarded as an essential defence mechanism in Chagas's disease, there is also evidence of the effect of humoral factors on the trypanosomes. However, antibodies could not be detected throughout the whole infection. In contrast to the mice, the A-C rats were highly resistant to infection, the resistance increasing with age from 100 days onwards. The infection proceeds by crises, after which the acute phase subsides, and the infection becomes chronic. During the crises, phagocytosis in the inflammatory nodules, correlated with an increase in the antibody titre, is a factor determining the turning point in the infection. It was shown that immunization with attenuated cultures produced a much higher degree of protection against re-infection than inoculation of trypanosomes with primaquine, and that cortisone, when administered early and in high dosage, inhibited the development of immunity.

C. A. Hoare

Knierim, Feliza. Estudio serológico en animales experimentalmente infectados por *Trypanosoma cruzi*. [**Serological Study in Animals experimentally infected with** *Trypanosoma cruzi*] *Bol. Chileno de Parasit.* 1954, Jan.–Mar., v. 9, No. 1, 2–6. English summary.

The author describes investigations on various serological reactions in laboratory rodents infected with *Trypanosoma cruzi*. In this study the presence of precipitins was determined by the ring test, by means of the polysaccharide haptene of the trypanosome antigen, prepared by Muniz's method [this *Bulletin*, 1948, v. 45, 54]. Agglutinins were determined by Senekjie's [*ibid.*, 1943, v. 40, 681] and Hauschka's [*ibid.*, 1950, v. 47, 607] methods, with suspensions of living trypanosome cultures as antigen. The complement-fixation reaction was carried out with various dilutions of serum against antigen prepared by the Freitas-Almeida method [*ibid.*, 1949, v. 46, 1129]. The results were as follows: (a) no antibodies for *T. cruzi* could be detected either in normal or infected mice; (b) agglutinins were present in normal rats, increasing in titre during the acute phase of the infection up to the 20th day, and diminishing as it became chronic; the precipitin and complement-fixation tests in this animal reacted positively

during the acute stage, and remained at a high titre in the chronic stage; (c) in guineapigs natural agglutinins were absent, but they made their appearance during the acute phase of the infection, after which they diminished in potency; the complement-fixing antibodies developed late in the acute phase and showed a low titre when the infection became chronic.

It is pointed out that the correlation established between the serological reactions and the resistance of the above-named rodents to infection with *T. cruzi* emphasizes the important part played by humoral factors in the defence mechanism against experimental Chagas's disease. *C. A. Hoare*

FEVERS OF THE TYPHUS GROUP

In this section abstracts are arranged as far as possible in the following order:—general; louse-borne typhus, flea-borne typhus, mite-borne typhus; rickettsialpox; tick-borne typhus; Q fever, other rickettsial diseases.

Rosenberg, S. & Bovarnick, Marianna R. **Isolation of the Rickettsial Inhibitor from Autoclaved Diphosphopyridine Nucleotide.** *J. Biol. Chem.* 1954, Dec., v. 211, No. 2, 763–72, 2 figs. [20 refs.]

"The main products formed by autoclaving diphosphopyridine nucleotide have been isolated by ion exchange chromatography and have been identified as nicotinamide and adenosine diphosphoribose. Traces of adenine and adenylic acid are also produced and a small amount of DPN may remain unaffected.

"Adenosine diphosphoribose was found to inhibit the action of DPN in typhus rickettsiae and in an isolated enzyme system requiring DPN. With the enzyme system used, this inhibition was competitive. With the rickettsiae, the inhibition of DPN by ADPR accounted for the inhibition found with autoclaved DPN."

Bovarnick, Marianna R. & Allen, Emma G. **Reversible Inactivation of Typhus Rickettsiae. I. Inactivation by Freezing.** *J. General Physiol.* 1954, Nov. 20, v. 38, No. 2, 169–79, 1 fig. [14 refs.]

Typhus rickettsiae suspended in normal saline were found to be damaged by alternate freezing and thawing; the damage consisted in a reduction of their haemolytic activity, toxicity and infectivity. When the damaged rickettsiae were incubated in a medium containing diphosphopyridine nucleotide (DPN) for 2–3 hours at 34°C. there was a considerable degree of restoration of these activities, sometimes as much as ten-fold, though in most cases they were still only a fraction of their original strength. When coenzyme A was added to the medium in addition to DPN there was some increase in the degree of restoration.

Rickettsial suspensions made with normal sucrose, instead of normal saline, suffered less damage from freezing and thawing.

DPN was found to be normally present in rickettsial suspensions and to be inactivated by freezing the suspension when made with isotonic saline.

The reversibility of the damage done by freezing and thawing is regarded as a remarkable phenomenon which may have an important bearing on the

reliability of determinations of the number of viable organisms contained in suspensions or other infected materials.

Other recorded examples of reversible loss of activity among micro-organisms are referred to and discussed. *John W. D. Megaw*

Wojciechowski, E. & Mikołajczyk, E. Działanie chloromycetyny na *Rickettsia prowazeki*. Porównanie 3 preparatów chloromycetyny. [**Action of Chloromycetin on *Rickettsia prowazeki*. A Comparison of Three Preparations of Chloromycetin**] *Med. Dośw. i Mikrob.* Warsaw. 1954, v. 6, No. 3, 293–8. English summary.

A preparation of *Rickettsia prowazeki* from louse gut was mixed with chloramphenicol in a final concentration of 1 mgm. per cc. and inoculated into lice as a test of infectivity after incubation at 20–24°C. for periods of up to 18 hours. The results showed that the rickettsiae were inactivated by exposure to chloramphenicol for 17 hours. A reduction in infectivity was observed in further experiments in which rickettsial suspensions mixed with chloramphenicol in final concentrations of 0·5 to 2 mgm. per cc. were inoculated into the yolk sac of fertile eggs on the 6th day of incubation. *D. J. Bauer*

Mathur, T. N. **An Outbreak of Typhus Fever in Simla.** *Indian J. Med. Sci.* 1954, Nov., v. 8, No. 11, 784–92, 799, 2 figs.

In the outbreak of typhus fever described in this paper 20 persons were attacked within 14 days in December 1952, in Simla, a hill station on a spur of the Himalayas. Seventeen of the patients were labourers from Kashmir who had been living with 120 others in grossly overcrowded conditions in a mosque situated in the bazaar of the town at an altitude of about 7,500 feet. The weather is described as being very cold; this is the normal condition in the winter months in Simla. The clinical and serological features of the cases were consistent with the diagnosis of louse-borne or flea-borne typhus but the author mentions only two points which he regards as being in favour of the louse-borne disease. These are the climatic and hygienic environment. In favour of murine typhus he states that the mosque is situated in the shopping centre of Simla, and was heavily infested with rats; that none of the many persons with whom the patients came into contact was attacked; that no louse infestation was found among the patients when they were admitted to hospital; that more cases would have been expected to occur among 137 persons living in close contact with one another if the disease had been louse-borne; and that " the disease was confined chiefly to one institution which shows it was murine typhus ". It is mentioned, however, that the cases may possibly have been of epidemic typhus started by a case of Brill's disease and that the failure of the outbreak to affect more than 16 per cent. of the persons at risk in the mosque may have been due to immunity of the Kashmiri labourers, resulting from previous attacks in their native country or to the low density of the louse population. The latter view is most likely to find general acceptance although the author concludes that " epidemiologically the cases appeared to be of murine typhus ".

There were only 2 deaths among the 20 patients, but 17 were treated with chloramphenicol or aureomycin [chlortetracycline], the total dosage of the latter ranging from 5 to 11·5 gm. except in one case in which the patient was apparently well after receiving 2·0 gm. but died suddenly.

Mention is made of a previous outbreak of typhus fever in Simla in 1923 when 16 cases occurred in a single family and 5 of the patients died; this outbreak appears undoubtedly to have been one of epidemic typhus.

John W. D. Megaw

Carrizosa, D. Brote de tifo ocurrido en Arócutin, Mich. Diciembre de 1953. [**An Outbreak of Louse-Borne Typhus in Arócutin, Michoacán, Mexico**] *Bol. Epidemiológico.* Mexico. 1954, Jan.–Mar., v. 18, No. 1, 1–6, 3 figs. & 1 chart.

An outbreak of louse-borne typhus is described. There were 38 cases of which 4 were fatal; 22 of the cases occurred in the village of Arócutin in the state of Michoacán, in Mexico. The village has a population of 284. It is situated at an altitude of about 2,000 metres so that although the affected area is in the tropical zone the climate is not tropical. The average mean temperature is 15·9°C. and there is a cold season in which the absolute minimum temperature falls as low as 2°C. The present outbreak occurred in the winter and early spring and therefore conformed to the traditional rule that louse-borne typhus is essentially a disease of cool or cold weather such as occurs even in the tropics in upland situations.

John W. D. Megaw

Mathur, T. N. **The Nature of X 2 Typhus in the Punjab. Report of Three Cases.** *Indian J. Med. Sci.* 1954, Nov., v. 8, No. 11, 779–83, 2 figs.

The author describes and discusses three cases of fever of the typhus group which occurred in the Punjab (India).

In the first case there was a history of bite by an " insect ", which was believed to be a tick; there was associated lymphadenitis. A generalized papular rash extended to the palms and face; a few of the spots were haemorrhagic. The Weil-Felix reactions on the 11th, 18th, and 22nd days, respectively, were as follows:—with *Proteus OX2*, 1 in 125, 1 in 250, and 1 in 125; with *P. OX19* on the corresponding days they were 0, 1 in 83, and 0. Tick typhus was suspected but the complement-fixation reaction with this antigen was negative and with murine typhus it was positive at 1 in 32.

In the second case there was a conspicuous papular rash which did not extend to the palms, soles, or face. The *P. OX2* reaction was negative on the 12th day, but rose to 1 in 125 on the 27th day; with *P. OX19* the reaction was negative on both these days. The complement-fixation reaction was positive at 1 in 8 with tick-typhus antigen and negative with epidemic typhus and murine typhus antigens.

In the third case both the *OX2* and *OX19* reactions were positive at 1 in 125 on the 11th, 13th and 18th days; the titre of both reactions was 1 in 83 on the 40th day. The complement-fixation test with murine-typhus antigen was positive at titres rising from 1 in 8 (+) to 1 in 16 (++); with tick-typhus antigen the reaction was presumably negative as the diagnosis was murine typhus.

[The name " *X2* typhus " is not a suitable synonym for tick-borne typhus in which agglutination of the *P. OX19* type is quite as common as that of the *P. OX2* type in the U.S.A. and South Africa (see Gear quoted in this *Bulletin*, 1955, v. 52, 261). The name " *OX19* typhus " is even less suitable: this type of reaction may occur in louse-borne, flea-borne, and tick-borne typhus.]

John W. D. Megaw

Saint, E. G., Drummond, A. F. & Thorburn, I. O. **Murine Typhus in Western Australia.** *Med. J. Australia.* 1954, Nov. 6, v. 2, No. 19, 731–7, 13 figs. (5 on pl.). [35 refs.]

The authors give a good general description of murine typhus in Western Australia where 1,332 cases, of which 50 were fatal, have been notified during the 26 years, 1927–1952. Till 1942 the average yearly number of cases was about 30, but in 1943 it suddenly rose to about 120, and during the next 6 years it varied within the range 60 to 140; in 1950–1952 it has been rather below the pre-war figure.

Most of the cases occurred in Perth and Freemantle; in these cities, as in the rest of the State, the incidence has been definitely associated with the degree of rat infestation. In a number of cases there was strong circumstantial evidence pointing to infection by the inhalation of contaminated dust in rat-infested buildings.

Among 22 cases in which the chest was examined by X-rays there was evidence of pneumonitis in 5. For the diagnosis special reliance was placed on the Weil-Felix test. The provisional diagnosis before receipt of the laboratory report was correct in only 40 per cent. of the cases.

The treatment of 11 of the patients studied was by one or other of the broad-spectrum antibiotics and as usual the results were excellent except in one case in which there was no rash but the Weil-Felix titre rose from zero to 1 in 400. In 2 other cases the treatment was started on the 5th day and was continued for 4 days; it consisted of a loading dose of 3·0 gm. followed by doses of 0·5 gm. every 6 hours. Both of the patients responded in the usual way but relapsed within 4 days of receiving the last dose. The authors' comment is: "When treatment is begun before antibodies have reached their peak, it should be continued for at least four or five days after the fall in temperature". [This would involve a total dosage of 14–18 gm. and the question arises whether it would not be preferable in such cases to adopt the usual system of dosage, follow this by a period of 3–4 days' rest, and then give a short further course lasting about 2 days. The broad-spectrum antibiotics, being only rickettsiostatic, cannot be expected to be curative by themselves, and in heavy doses they may inhibit the production of the immunizing antibodies which are the essential factors in producing a lasting cure. In any case the relapses that so often occur after antibiotic treatment in the early stages of the rickettsial fevers do not seem to be of great importance; they respond to short courses of the drugs.] *John W. D. Megaw*

Audy, J. R. & Nadchatram, M. **A Method of rearing Individual Trombiculid Mites in the Field.** [Correspondence.] *Nature.* 1954, Nov. 27, v. 174, 1021–2.

The importance of post-larval characters in the taxonomy of Trombiculid mites (Acarina: Trombiculidae) has been recognized since the pioneer work of Womersley [this *Bulletin*, 1952, v. 49, 942]. Very often a single host may carry more than one species of mite larvae and it may be possible to determine the species accurately only by rearing the larvae individually to the nymphal stage and studying the nymphal characters. These can then be correlated with the larval characters as observed in the larval pelt. In the field, when the acarologist is on the move, rearing the mites may be a difficult matter and the method described in this note is designed to overcome this difficulty.

The engorged larva is placed on a strip of cigarette paper on which the

collection data are written down. This is then introduced into a length of glass tubing (35 mm. × 8 mm.) after being thoroughly wetted. The tube is closed at both ends by soft rubber corks. Several such tubes with single larvae can be stored and carried about. When the nymph emerges it is preserved in 50 per cent. spirit. The larval pelt which remains attached to the paper can be floated off in water, mounted and studied.

M. G. R. Varma

Price, W. H. **The Epidemiology of Rocky Mountain Spotted Fever. II. Studies on the Biological Survival Mechanism of** *Rickettsia rickettsii*. *Amer. J. Hyg.* 1954, Nov., v. 60, No. 3, 292–319, 1 fig. [29 refs.]

This is a very useful and interesting contribution to knowledge of the epidemiology of tick-borne typhus of the Rocky Mountain spotted fever type. It deals specially with the disease in the eastern part of the United States where its existence was not detected till 1931 although its essential epidemiological features had been established by the brilliant work of Ricketts in the western U.S.A. as early as 1909, and Wolbach's classical monograph on the subject had been published in 1919 [this *Bulletin*, 1920, v. 16, 420]. It has been suggested by the reviewer and other workers that the inordinate delay in recognizing the existence of tick-borne typhus in many parts of the world, including the eastern United States, may have resulted from the misleading suggestion contained in the name Rocky Mountain spotted fever. Even when the disease was recognized in the eastern states it was regarded as being different in type from the western disease, but the author points out that there is no justification for applying the distinctive name "eastern type of spotted fever" because strains of similar low virulence have been found by Topping [*ibid.*, 1942, v. 39, 148] and himself [*ibid.*, 1954, v. 51, 44] in the western part of the United States, and highly virulent strains have been found in Washington and Georgia.

The present paper deals with the epidemiology of the disease in Maryland from 1931 to the end of 1950. In the 4 successive periods of 5 years from 1931 the numbers of cases reported from Maryland have been, respectively, 150, 235, 273, and 313. The average fatality rate was 17·1 per cent., ranging from less than 10 per cent. among persons under the age of 25 to about 60 per cent. for those over the age of 60. More than half the patients were less than 15 years old, the highest incidence being in the 5–9-years age-group. The fatality rate remained fairly constant till 1949 when it dropped suddenly with the introduction of the broad-spectrum antibiotics. Among the 112 cases reported in 1949 and 1950 there were only 3 deaths, whereas among the same number in the years 1942 and 1943 there were 28 deaths. As many as 93 per cent. of the cases occurred in the 6 months, April to September, the peak incidence being in July. In the Mountain and Pacific states the season of high incidence begins and ends about one month earlier.

Studies of the virulence of the rickettsiae and of the relationship between the animal hosts and arthropod vectors are described in detail; these will be found very helpful by workers who undertake surveys of areas in which tick-borne typhus is known or suspected. A few examples of the findings are as follows. Dogs and field mice (*Microtus pennsylvanicus*) appeared to be important reservoirs of infection in the area. Among 28 patients investigated in the field 20 were found to own dogs, and in 10 of these cases *Rickettsia rickettsi* was isolated from *Dermacentor variabilis* ticks found on the dogs. Attacks were commonly associated with the removal of ticks

from dogs 5–14 days before the onset of the attacks. Wild rabbits did not appear to play an important part in maintaining infection in Maryland. Their principal tick, *Haemaphysalis leporis-palustris*, yielded strains of rickettsiae which always behaved quite differently from those isolated from man or from *D. variabilis*. In one endemic area about 3,000 *D. variabilis* ticks were collected by flagging in each of 3 consecutive years; in 1951 and 1952 *R. rickettsi* were isolated from 0·3 per cent. of the ticks and in 1953 from 0·2 per cent. The virulence of *R. rickettsi* recovered from *D. variabilis* was always increased by 1–3 passages through chick embryos or by one passage through man. Experimental tick-to-tick transmission through field mice was possible with larval or nymph forms of *D. variabilis*; transmission through dogs was by adult ticks. The mice and dogs remained infective to uninfected ticks for a period of about a week. The virulence of *R. rickettsi* tended to fall during multiplication in natural animal hosts and to rise during multiplication in the tick.

All the strains isolated in Maryland were of the low-virulent type.

In favourable conditions 76–81 per cent. of larvae and nymphs of *D. variabilis* became infected by feeding on infected *Microtus pennsylvanicus*, and 82 per cent. of the adult ticks of this species became infected by feeding on infected dogs. The low-virulent strains died out after 14–16 months in *D. variabilis* under conditions simulating those occurring in nature, and even towards the end of this period the virulence remained the same. Transovarial transmission occurred in " 30 to 40 per cent. of the time " in *D. variabilis*. A variable proportion of the individual eggs, 1 in 20 to 1 in 2, became infected. Every infected egg gave rise to an infected larva, nymph, and adult tick.

In a note added after the paper was written it is stated that an article has appeared which described the first clear-cut isolation of *Rickettsia rickettsi* from a wild animal in North America; the animal was *Microtus pennsylvanicus* [see this *Bulletin*, 1954, v. 51, 906].

John W. D. Megaw

Raška, K., Aldová, E., Kubásek, M., Syrůček, L., Havlík, O., Manych, J. & Šána, B., with the technical assistance of A. Neubertová, A. Vejtrubová & H. Zeníšková. Q horečka. Sdělení 1. Zpráva o prvých u nás pozorovaných epidemiích. [**Q Fever. I. The First Epidemic observed in Czechoslovakia**] *Časopis Lékařů Českých*. Prague. 1954, Oct. 15, v. 93, No. 42, 1153–5.

Six cases of Q fever occurred in May 1953 among persons working on a state farm in an isolated community in Czechoslovakia. The epidemic continued until the middle of June, and 15 cases occurred in all; the infection was derived from cattle, and the diagnosis was established by complement-fixation tests. Two other cases in human beings occurred in June 1953 in a village 10 km. away, and epidemiological investigation revealed that 35 cases of Q fever had occurred in farm workers in January and February 1953 at a time when the flocks of sheep were being affected by the disease. An epidemic of 13 cases occurred in December 1953 in a community situated over 30 km. away from the other two localities, and an epidemic of 6 cases occurred in another place in April 1954, the infection in the 2 outbreaks being derived from cows. In the spring and summer of 1954, 30 cases of Q fever occurred among farm workers in another locality, and serological investigation showed that 55 persons had been affected in all. Seven strains of *Rickettsia burneti* were isolated from patients during the various outbreaks.

D. J. Bauer

Combiescu, D., Saragea, Alice & Esrig, Mira. Cercetări experimentale şi epidemiologice asupra tifosului pulmonar (febra "Q"). IV & V. [**Experimental and Epidemiological Studies on Q Fever. IV. Infection of Guineapigs by Instillation of** *R. burneti* **into the Conjunctival Sac. V. Infection of Guineapigs by the Cutaneous Route with Pathological Material containing** *R. burneti*] *Studii şi Cercetări Inframicrobiol., Microbiol. şi Parazitol.* 1953, July–Dec., v. 4, Nos. 3/4, 381–7, 2 figs. French summary.

The authors were able to infect guineapigs by the conjunctival route, with instillations of spleen suspensions from guineapigs infected with *R. burneti*. They also found that while it was possible to infect guineapigs with epidemic typhus alike through the shaved, scarified skin and through the depilated or normal skin, infection with *R. burneti* occurred only when the pathological material was placed on the shaved and scarified skin.

This difference is attributed largely to a difference in the infecting doses contained in the material used. In the case of the epidemic typhus study, lungs of mice inoculated intranasally were found to contain about 8,000 million infecting doses, while guineapig spleens infected with *R. burneti* contained only a few hundred or, at most, a few thousand infecting doses.

H. J. O'D. Burke-Gaffney

YELLOW FEVER

In this section abstracts are arranged as far as possible in the following order:—epidemiology. aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control.

Beet, E. A. **Encephalitis after Yellow Fever Vaccination.** [Correspondence.] *Brit. Med. J.* 1955, Jan. 22, 226–7.

In this communication the author records the occurrence of a case of encephalitis following the inoculation of a 3-month-old baby boy with 17D virus vaccine. The child who, while in the United Kingdom in 1954, had been vaccinated against smallpox on 30th October and against yellow fever on 22nd November, arrived by air on 30th November at Kano, Nigeria. On 3rd December, because of his refusal to take his feeds, he was admitted to hospital. On 4th December, *i.e.*, 12 days after his yellow fever vaccination, his rectal temperature was 103°F. (39·5°C.); he developed a Jacksonian attack involving the left limbs; this was accompanied by a left facial palsy and deviation of the eyes to the left. Recovery was uneventful.

[Between 1952 and 1954 nine previous cases of encephalitis associated with the use of 17D virus vaccine had been reported: 6 in France between August 1952 and December 1953, and 3 in England between November 1953 and October 1954. Of the 6 cases in France record of five was made by Lépine, quoted by Stuart (this *Bulletin*, 1955, v. 52, 143), and of one by Lartigaut and Couteau (*ibid.*, 147); of the 3 cases in England record was made of the first by Smith, of the second by Haas, and of the third by Scott (*ibid.*, 37).] *G. Stuart*

See also p. 337, Giglioli, **Residual Effect of DDT in a Controlled Area of British Guiana tested by the Continued Release of** *Anopheles darlingi* **and** *Aedes aegypti*: **a Practical Technique for the Standardized Evaluation of Over-All Residual Efficiency under Field Conditions.**

DENGUE AND ALLIED FEVERS

Sweet, B. H. & Sabin, A. B. **Properties and Antigenic Relationships of Hemagglutinins associated with the Dengue Viruses.** *J. Immunology.* 1954, Nov., v. 73, No. 5, 363–73, 3 figs. [16 refs.]

This paper will appeal specially to workers who are interested in the specific haemagglutinins for chick, pigeon, or sheep erythrocytes which have been found in extracts of mouse brains infected with a great variety of viruses, including those of yellow fever and of a mouse-adapted strain of Sicilian sandfly fever.

In this paper the authors describe the recovery of distinct haemagglutinins from the brains of suckling mice infected with 2 immunologically distinct strains of dengue virus. The strains of dengue virus studied were one from Hawaii (Type 1) of the 7th and 118th mouse passage, and one from New Guinea (Type 2) of the 19th mouse passage.

Haemagglutinin of Type 2 virus was demonstrable when chick erythrocytes were allowed to sediment at 4°C. at *p*H 6·5–6·7 only, but not at 20–25°C. whereas Type 1 haemagglutinin of 7th and 118th mouse passages was demonstrable at 4° and 20–25°C. and at a wider range of *p*H (6·2–7·5); the maximum titre being at *p*H 6·7. Both types of haemagglutinins deteriorated rapidly at *p*H 6·7 at temperatures of 4°, 25°, and 37°C.; unexpectedly the deterioration was most rapid at 4°C. At *p*H 7–7·9 both types were stable at 4° and 25°C., but at 37°C. Type 1 of the 7th mouse passage and Type 2 remained stable for at least 18 hours, whereas Type 1 of the 118th mouse passage became almost inactive within 1 hour.

At *p*H 7·9 and 4°C. all the varieties of haemagglutinins remained stable for at least 4 months but all were completely inactivated when thawed out after freezing at about −80°C.

An antibody having a specific haemagglutination-inhibiting effect (H-I) was readily separated by precipitation with acetone from the normal inhibitor occurring in sera of man, monkey, and rabbit. By H-I tests it was found that the dengue viruses were antigenically related to the St. Louis, Japanese B., West Nile, and yellow fever viruses, but not to the viruses of sandfly fever, Rift Valley fever, or western equine encephalitis. Details of the methods employed in the study and a discussion of the whole subject of the haemagglutinins are given in the paper. *John W. D. Megaw*

RABIES

Bartmann, K. Jahresbericht der Wutschutz-Abteilung des Robert Koch-Institutes, Berlin, für 1952. [**Annual Report for 1952 of the Rabies Prophylaxis Department of the Robert Koch Institute, Berlin**] *Zent. f. Bakt.* I. Abt. Orig. 1954, v. 161, No. 6, 342–8.

No annual report of the work of the Rabies Department of the Robert Koch Institute has appeared since 1939 but the spread of an epizootic of rabies from eastern Europe into parts of Germany since 1949–1950 [this *Bulletin*, 1954, v. 51, 568] has made the present report necessary. During 1952 a total of 5,305 persons who feared the possibility of their infection with rabies were investigated. These persons are grouped into a number of categories including those in which rabies infection was definitely

diagnosed or suspected, or in which it was not found, in the suspected animals. Some particulars are given of the nature of the lesions caused by the large variety of animals suspected of having the disease. Partial or complete courses of prophylactic inoculation were carried out according to the results of the investigation of the circumstances of the lesions sustained. Full treatment was given to 1,330 persons—1,194 by the method of Semple and 136 by that of Hempt. Details are given of the methods used in the preparation and administration of these 2 prophylactics. During 1952, 3 deaths from rabies in persons who had not been inoculated were reported to the Department. *M. E. Delafield*

Boulger, L. R. & Cannon, D. A. **The Effect of Temperature on the Keeping Properties of Rabies Vaccine, prepared at Yaba, Nigeria.** *West African Med. J.* 1954, Dec., v. 3 (n.s.), No. 4, 162–5, 1 graph.

This paper gives details of experiments carried out by the authors to determine the effect of storage at different temperatures on the antigenic potency of a Semple-type antirabies vaccine—a 4 per cent. tissue suspension in 0·5 per cent. phenolized physiological salt solution of emulsified brain from sheep inoculated with fixed rabies virus (Pasteur strain). For the assessment of potency a slight modification of the Habel test was employed. Results showed that vaccine, when stored at 2° to 5°C., retained a satisfactory level of antigenicity for a period of 6 months; when stored at room temperature (24° to 32°C.), it failed to retain its antigenic potency for more than one month, unless it had been originally of a high protective value (*e.g.*, 46,000 MLD), and even so it proved to be antigenically unsatisfactory by the end of 2 months; when stored at −4° to 0°C., it very rapidly lost its immunizing power, one batch, for example, with a protective value of 60,000 MLD, revealing only a trace of antigenicity after one month in the frozen state. [That phenolized antirabies vaccine should not be frozen at any time during its preparation or storage has been stressed by Lépine and Béquignon and by Kaplan [*WHO Monograph Series No. 23*: this *Bulletin*, 1954, v. 51, 1242]; these authors also prescribe for the vaccine a storage temperature of 2° to 5°C. at all times during its period of use, *i.e.*, during the 5 or 6 months following the date of manufacture or date of issue.] *G. Stuart*

Banerjea, J. C. & Maiti, C. R. **Ascending Myelitis following Anti-Rabies Inoculation with a Report of Two Cases and a Short Review of Literature.** *Calcutta Med. J.* 1954, Sept., v. 51, No. 9, 287–91. [35 refs.]

In this article the authors, after briefly reviewing the literature on neuroparalytic accidents complicating antirabies treatment in general, provide a detailed account of two cases of ascending myelitis, which followed the use of 5 per cent. Semple-type vaccine in India. In one case paralytic manifestations appeared 23 days after the last of the prescribed 14 daily injections of 5 cc. of the vaccine had been given; in the other case they appeared on the 11th day of treatment, *i.e.*, after the 11th injection. In the first of these cases the patient, a 44-year-old male, died 32 days after the onset of symptoms; in the second case the patient, a 20-year-old male, made a delayed but incomplete recovery: on discharge from hospital 66 days after the onset of symptoms, he was able to walk only with the aid of a stick; his limbs were still flaccid; there was no response to superficial reflexes; and urine was passed with difficulty.

In their commentary the authors warn against the indiscriminate use of antirabies vaccine; accept, in explanation of the occurrence of such neuroparalytic accidents, the theory of an anaphylactic reaction first advanced by Harvey and McKendrick; regard the use of corticotrophin, because of its known anti-allergic action, as of promising value in the therapy and control of these accidents, particularly those of the encephalomyelitic group; and recall that the risk of accident is reported to have been lessened by the administration of hyperimmune antirabies serum, followed by only 7 injections of 5 per cent. Semple-type vaccine.

[The advantages of antirabies serum used either alone or in conjunction with vaccine—a combination which reduces the amount of vaccine necessary and thus the risk of paralytic accidents—have been emphasized by Habel (this *Bulletin*, 1954, v. 51, 1239).] *G. Stuart*

Piringer, W. & Sarmiento, J. Tuberkulose, Kontraindikation gegen eine antirabische Vaccination? [**Does Tuberculosis Contraindicate Vaccination against Rabies?**] *Arch. f. Hyg. u. Bakt.* 1954, Dec., v. 138, No. 8, 591–8. [33 refs.]

The authors, from Bogotá, Colombia, describe at length the occurrence of paralysis after antirabic vaccination in a man of 37 who had received a full course of 5 per cent. Semple-type vaccine. He had suffered from tuberculosis in his youth, but this was now healed. The paralysis occurred 13 days after the rabies vaccination. The authors therefore vaccinated in the same way 23 rabbits previously infected with *Myco. tuberculosis*, H 37 Rv. No neurological or other accidents occurred.

The authors discuss the implications of this occurrence and conclude that while a history of tuberculosis does not contra-indicate a necessary vaccination against rabies, particular care should be taken and the patient should preferably be kept in bed throughout. *H. J. O'D. Burke-Gaffney*

PLAGUE

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, rodent hosts, transmission, pathology, diagnosis, clinical findings, treatment, control.

Jesierski, A., Fain, A. & Devignat, R. Isolement au Congo Belge, à partir du cheval, d'une souche insolite de *Pasteurella pestis* var. *orientalis*. [**The Isolation of an Unusual Strain of** *Pasteurella pestis* **var.** *orientalis* **from a Horse in the Belgian Congo**] *Ann. Soc. Belge de Méd. Trop.* 1954, Aug. 31, v. 34, No. 4, 469–73.

The authors describe the isolation of a strain of *Pasteurella pestis* var. *orientalis* from the nasal mucus of a horse in Elisabethville in October 1950. The horse had been slaughtered because of a swelling of the skull which was attributed to osteoporosis, and organisms resembling *P. pestis* were seen in stained smears of the nasal mucus. Similar organisms were isolated from guineapigs inoculated with suspensions of the spleen and lymphatic glands of the horse. On culture the organisms were found to correspond to the local strains of *P. pestis* except that they did not ferment glycerin and that they were avirulent to guineapigs and rats. Detailed study of the sugar and other reactions showed complete agreement between them and an avirulent

strain of *P. pestis* var. *orientalis* used for immunization. This finding was confirmed by GIRARD who added that the strain protected guineapigs better than mice and that it resembled the vaccinating strain " E.V." of GIRARD and ROBIC.

Although the strain undoubtedly came from the horse it cannot be said with certainty that it caused the disease from which the horse was suffering. Up to the present time neither human nor murine plague has been detected in the region of Upper Katanga where the event occurred, and the only previous reports of plague infection in large domestic animals are the finding of the disease in the camel by KLODNITSKY in 1918 and among asses in 1910–1911 by FUJINAMI during the great epidemic in Manchuria.

John W. D. Megaw

MACCHIAVELLO, A. **Reservoirs and Vectors of Plague.** *J. Trop. Med. & Hyg.* 1954, Jan., v. 57, No. 1, 3–8. [12 refs.] *Ibid.*, Feb., No. 2, 45–8. *Ibid.*, Mar., No. 3, 65–9. *Ibid.*, Apr., No. 4, 87–94. *Ibid.*, May, No. 5, 116–21. [43 refs.] *Ibid.*, June, No. 6, 139–46. *Ibid.*, July, No. 7, 158–71. *Ibid.*, Aug., No. 8, 191–7. *Ibid.*, Sept., No. 9, 220–24. *Ibid.*, Oct., No. 10, 238–43. *Ibid.*, Nov., No. 11, 275–9. *Ibid.*, Dec., No. 12, 294–8.

This series of 12 articles on the reservoirs and vectors of plague has been published in monthly instalments in the *Journal of Tropical Medicine and Hygiene* for 1954. It is described by the author as a revision and expansion of the preliminary list which he submitted to the first meeting of the Expert Committee on Plague, WHO, in September 1949; this was prepared as a working document in mimeographed form under the name *Nomenclature of Reservoirs and Vectors of Plague*. The present list has been published because of the need for periodic revision of papers of this kind. It is now possible to revise the names of the vectors so as to conform with the nomenclature adopted in the Catalogue of the Rothschild Collection of Fleas by HOPKINS and ROTHSCHILD, of which the first volume dealing with the Pulicoidea has appeared in 1953 [this *Bulletin*, 1953, v. 50, 1183], and the names of the other fleas have been revised by Hopkins so that they now conform to the most authoritative nomenclature.

For each of the vector fleas references are given to the taxonomic determination, the original description, the worker who proved its infection or its vector capacity, with the date and place of the finding. For the animal reservoirs corresponding information is given.

The flea vectors are listed under 4 heads (a) cosmopolitan fleas, of which there are 7; (b) vectors of limited habitat; there are 53 of these which are arranged according to the country of origin; (c) fleas found spontaneously infected, exclusive of those with proved vector capacity; and (d) fleas experimentally infected, excluding those found spontaneously infected or proved vectors. Altogether 101 species of fleas are included in these lists.

The rodents and other animals found naturally infected with plague or experimentally susceptible of infection are listed separately for each of the chiefly affected geographical regions, including Africa, America, Asia, Russia, and Oceania. Altogether 372 species of animals are mentioned and, when available, lists are given of the fleas infesting each of them. Other tables deal with a general index of plague-infected Siphonaptera and their geographical distribution, an alphabetical index and host distribution of these Siphonaptera, an index of plague-infected animals, and one of plague-infected rodents showing their known geographical distribution.

The author classifies flea-transmitted plague as (a) Port and Urban

Plague and (b) Sylvatic Plague; he defines the former as occurring throughout the world as a primary disease of *Rattus*, transmitted to man by very few species of vectors, of which *Xenopsylla cheopis* and *Nosopsyllus fasciatus* are the only ones of real importance; the latter is described as a local enzootic phenomenon of which there are as many forms as there are foci of the disease.

[It is very unfortunate that these articles could not have been published in book form. They would have been a valuable addition to the books on plague on a library shelf; in their present form they are very inconvenient for consultation and are likely to escape the notice of many who would find them very useful as sources of reliable information on the reservoirs and vectors of plague.] *John W. D. Megaw*

KARTMAN, L. **Studies on *Pasteurella pestis* in Fleas. I. An Apparatus for the Experimental Feeding of Fleas.** *Exper. Parasit.* New York, 1954, Nov., v. 3, No. 6, 525–37, 3 figs. [32 refs.]

The author first reviews the literature on the techniques for the *in vitro* feeding of haematophagous arthropods and then describes an apparatus which he has designed for the *in vitro* feeding of fleas. Photographs of the apparatus are presented, as also are preliminary data on feeding tests with the fleas *Xenopsylla cheopis* and *Malaraeus telchinum*.

It is suggested that the apparatus is suitable for use in an experimental approach to basic problems of flea physiology, nutrition and disease transmission. It contains at least two working units for comparing results and could be designed with any number of units according to need.

The skin of an appropriate host is prepared and stretched, and secured, smooth side outward, over one end of a transparent plastic tube. A stock of such tube-skin preparations from various host species is kept at approximately −50°C.; when needed they are thawed and dried.

Two or more heat-conducting tubes of brass or other metal are secured to a wooden block so that their lower ends dip into the water of a water bath running at 41°C. A circular metal dish containing blood is lowered on to the top of each conductor tube and a plastic sleeve is placed over them. One of the prepared plastic feeding tubes is lowered into each sleeve until the membrane rests upon the blood dish. The blood, which now has a temperature of approximately 37°C., spreads over the surface of the membrane and when the fleas are poured into the feeding tubes they begin feeding immediately.

Preliminary tests showed that the thinner skins of younger animals and the comparatively thin skins of small rodent species offered the best chances of good feedings. The age of the blood and the effects of freezing it had little influence.

Later observations showed that fleas will not feed through Cellophane whereas 68 out of 107 fed through a *Microtus californicus* skin. Fleas would feed as readily on a commercial preparation of human blood used for transfusions as they did on rat blood. *H. S. Leeson*

EHRENKRANZ, N. J. & WHITE, L. P. **Hepatic Function and other Physiologic Studies in Monkeys with Experimental Pneumonic Plague.** *J. Infect. Dis.* 1954, Nov.–Dec., v. 95, No. 3, 226–31, 4 figs.

In the experiments described in this paper 11 *Macaca rhesus* monkeys were inoculated by the intratracheal route with suspensions of a virulent strain of *Pasteurella pestis* for the purpose of studying the pathological

changes occurring in pneumonic plague. For a comparison of the effects of bubonic plague 7 other monkeys were inoculated intracutaneously with the same strain.

In attacks of pneumonic plague pronounced diminution of the liver function was shown to have occurred in nearly all of the monkeys by the second day of the fever, whereas in bubonic plague there was little evidence of abnormality during the first four days. The tests employed were the thymol-turbidity and the bromsulphthalein-retention reactions.

By cultural tests of liver substance obtained by biopsy it was found that *P. pestis* was present in the organ in most of the pneumonic cases by the second day of the fever and usually in considerable numbers; in the bubonic cases only 1 of 6 monkeys tested on the third to the fifth day gave a positive result and this consisted only of a single colony. It appeared that in pneumonic plague invasion of the liver, with functional disturbance, occurred early in the course of the attack and contributed to the fulminating course of the disease.

Other findings were that in pneumonic plague the systolic blood pressure was practically normal till just before death, that haemoconcentration was absent throughout the illness and that there was a conspicuous fall in the eosinophil count. These observations " imply that the adrenal cortex is able to maintain a hormonal response during the disease ".

John W. D. Megaw

Ransom, J. P. & Krueger, A. P. **Chronic Pneumonic Plague in** *Macaca mulatta*. *Amer. J. Trop. Med. & Hyg.* 1954, Nov., v. 3, No. 6, 1040–54, 8 figs. [18 refs.]

Three groups, each consisting of 8 monkeys (*Macaca mulatta*) were caused to inhale clouds of aerosol suspensions of various doses of a virulent strain of the 2nd passage of a 24-hour culture of *Pasteurella pestis*. The elaborate technical methods employed for regulating the number of organisms inhaled are described. It was estimated that the dosage ranged from about 24,200 to 112,000 bacilli. Three of the monkeys died between the 11th and 13th days, the remaining 21 survived for 15 or more days and were sacrificed at intervals during the 15–48-day period. From 2 monkeys, sacrificed on the 15th and 48th days, respectively, mouse-virulent and phage-sensitive *P. pestis* was isolated from the organs of the monkeys. In 3 other animals, sacrificed on the 15th and 20th days, the organisms were present in large numbers and were found to be characteristic of *P. pestis*, but were avirulent and not sensitive to phage.

At autopsy of the sacrificed monkeys anatomical lesions were found, which were regarded as those of chronic pneumonic plague, in about three-fourths of the animals. In a few cases there were focal lesions, about 2–3 mm. in diameter with necrotic centres surrounded by a zone of intense haemorrhage. In a single case there was hepatization of the involved lobe of the lung. In nearly half of the cases there was a dusky grey discoloration of the surface of the lung, sometimes in irregular streaks, sometimes spread all over the surface of the lung. In lungs studied in the late stages there was often a layer of coagulated exudate on the surface of the organ.

A detailed description, illustrated by 8 photomicrographs is given of the histological changes found in the lungs. In acute cases dense masses of bacilli were seen round the blood vessels; in chronic forms there were focal areas of mononuclear-cell infiltration. Damage to the vessel walls was a feature of most of the cases; this was associated with petechiae, ecchymoses or haemorrhage. Even in the late stages there were often active foci of tissue reaction in the lungs which were the chief sites of progressive damage

caused by multiplication of the bacilli. In the liver and kidneys there was no evidence of damage of this kind.

The relatively less severe course of the experimental disease in monkeys as compared with natural infection in man was attributed to the smaller number of viable organisms administered in the experiments.

John W. D. Megaw

CHOLERA

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

Bhaskaran, K. **Studies on *Vibrio* Dissociation. Part I. Smooth Rough Dissociation of *V. cholerae* in Rosaniline Agar.** *Indian J. Med. Res.* 1953, Apr., v. 41, No. 2, 143–57. [26 refs.]

The observation that certain batches of modified Aronson's medium were inhibitory to the growth of *V. cholerae*, and that the few resistant colonies that appeared, when heavy stroke cultures were made, were predominantly rough, has led the author to study the smooth-rough dissociation of *V. cholerae* using rosaniline as the dissociating agent. The modified Aronson's medium consisted of saccharose 2·0 per cent., sodium carbonate 0·4 per cent., sodium sulphite 0·12 per cent., and rosaniline 0·04 per cent. in Douglas agar (*p*H 7·8).

Nine strains of *V. cholerae* (4 Inaba, 4 Ogawa, and 1 Hikojima) isolated from actual cases of cholera were used. All strains were typical *V. cholerae* in morphology and biochemical activity save that the Hikojima strain was non-motile. Agglutination tests were carried out by Dreyer's method at 50°C., and rough were differentiated from smooth strains by Millon's test, the trypaflavin test, and agglutination by rough O serum. As it seemed that the inhibitory effect was due to precipitation of rosaniline by chemical reaction with sodium carbonate and basic fuchsin the amount of sodium carbonate in the medium was increased to 0·625 per cent.

The growth of all the strains of *V. cholerae* when inoculated on the basal Douglas agar was profuse and no rough colonies could be isolated. No constituent of the medium, when added by itself to the basal medium, was inhibitory and none produced rough colonies though the growth was less profuse with basic fuchsin. When basic fuchsin (0·04 per cent.) and sodium carbonate (0·625 per cent.) were added together the medium growth was much inhibited and the colonies which appeared were rough. Sodium sulphite (0·12 per cent.) on the one hand, and sucrose (2 per cent.) on the other, when added to the basal medium with basic fuchsin improved the growth but rough colonies were still produced. The addition of sodium sulphite to the other three suppressed the inhibitory effect and gave a profuse smooth growth. The rough change obtained in these experiments was not transitory but persisted through several subcultures on Douglas agar.

When rosaniline (BDH) was added as a fine watery suspension to Douglas agar (*p*H 9) in concentrations varying from 0·01 to 0·07 per cent. rough variants could be isolated in concentrations anywhere between 0·03 and 0·07 per cent. In concentrations lower than 0·03 per cent. no rough colonies could be isolated. There was no relationship between the degree of dissociation and the concentration of the dye. The *p*H of the basal medium could be varied from *p*H 8 to *p*H 10 without affecting the results.

Altogether 96 variants isolated on basic-fuchsin-sodium-carbonate agar (BC agar) from the 9 typically smooth strains of *V. cholerae* were studied. These variants showed every degree of dissociation, from typically rough strains, agglutinating only with rough O sera, to a few smooth strains which were unaffected by growing on the BC agar. The rough and smooth-rough (SR) variants retained their characteristics through several cultivations on Douglas agar and did not tend to revert to the parent strain. Some of the variants derived from Ogawa strains 49091 and 49109, possessed "trivalent agglutinative properties" [this *Bulletin*, 1948, v. 45, 334] agglutinating with Inaba, Ogawa, and rough O sera, but were stable in normal saline. No varient of the Ogawa strains behaved like a true Inaba. Many of the rough colonies were dry and brittle, but none was rugose in appearance or could be differentiated from smooth races by the appearance of the colonies. The pure rough strains were more unstable in salt solution than the intermediate varients but one rough strain was quite stable in M/2 NaCl solution.

Virulence tests were carried out by the intraperitoneal inoculation of mice with mucinized suspensions prepared from dilutions of 6-hour cultures in peptone water. The LD50, calculated by the method of Reed and Muench, varied from 0·000015 cc. to 0·00034 cc. of the culture. The rough variants were comparatively avirulent.

Agglutinating sera were prepared against one Inaba and one Ogawa smooth strain, and against rough and smooth-rough variants, and a trivalent variant; an antigenic analysis of these strains was carried out by complete reciprocal absorption tests. The results are shown in Table IV and reveal marked differences in O antigenic structure between smooth strains and their rough variants.

White showed that *V. cholerae* does not throw off rough variants spontaneously but only under the action of specific dissociating agents. Cholera phages, immune serum, glycine, alanine, lithium chloride, phenol, chlorine, and atebrin [mepacrine] have been employed for the purpose. The author does not claim that rosaniline is superior to these in producing dissociation but that its effect is more dramatic in that smooth strains became rough in 72 hours under its influence, and that no smooth strain failed to dissociate. Both basic fuchsin and rosaniline are inhibitory to *V. cholerae* but the colonies resistant to the former were quite smooth while those resistant to the latter were rough. This may be due to the difference in the chemical structure of the two dyes but other factors may be involved.

C. C. B. Gilmour

Chakravarti, H. S. & Chaudhuri, R. N. **Plasma Sodium, Potassium and Chloride Changes in Cholera and their Significance in Prognosis and Treatment.** *J. Indian Med. Ass.* 1954, Aug., v. 23, No. 11, 488–91.

Flame photometry has facilitated the estimation of plasma sodium and potassium and enabled serial estimations of these electrolytes to be made in various diseases. Of such studies in cholera, however, this is among the first. In 6 patients examined before any treatment had been given, the plasma sodium and chloride values were within the normal range and remained so during each of 5 successive days on which the estimations were repeated and during which intravenous saline was being administered. The plasma potassium value on admission was high in 4 cases but became normal or low in the course of treatment with intravenous saline infusions. In 2 cases it was below normal by the fifth day of treatment.

Of 8 fatal cases due to uraemia and pulmonary oedema in all of which standard treatment with saline had been administered, plasma sodium

values within 24 hours of the death of the patient were low in 5; in the remaining 3 large quantities of saline had been given in an effort to prevent circulatory collapse, the plasma sodium values were high, and death had resulted from pulmonary oedema. The plasma chlorides were not significantly abnormal in 7 cases, in one they were slightly low. In 6 the plasma potassium, and in all the blood urea, were abnormally high. In the 2 cases in which the plasma potassium was within the normal range exceptionally large quantities of saline had been given, and it was in these that the plasma sodium values were high.

The authors conclude that their observations support the hypothesis that in cholera the fluid lost from the body is isotonic with extracellular fluid and although the extracellular fluid remaining is much diminished in volume its isotonicity is well maintained. Its potassium content, however, increases and this increase possibly is a result of migration of potassium from the cells. They suggest that this may be provoked by an excess of acidity of the plasma and extracellular fluid which the potassium helps to neutralize. [A point which the authors do not bring out is that alteration in the permeability of the cell membrane itself may be responsible for the abnormal potassium values; there is evidence that such changes in permeability occur in conditions in which there is extracellular dehydration.] A further point discussed is that in cholera the concentration of protein in the plasma is much increased; such protein is weakly acidic and increases the total acidity of the blood. They also draw attention to the occurrence of uraemia in those cases in which there is pulmonary oedema, mentioning that if renal function is normal any excess of saline which is administered is readily eliminated and the danger of pulmonary oedema is therefore remote. Great care, however, is necessary in administering large quantities of saline if renal function is impaired.

In the fatal cases in which there was uraemia there was also a large increase in the plasma potassium. Failure of the kidney to excrete potassium probably contributed to this increase which was also aggravated by the amount of potassium liberated by tissue catabolism. The dangerously high level of potassium in the plasma which resulted may be one of the causes of the fatal termination. Measures to deal with this excess of potassium are outlined. [This is an excellent piece of work and the observations made are of great importance in the handling of patients suffering from cholera.] *A. W. Woodruff*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

EYLES, D. E. & JONES, Frances E. **The Prevalence of** *Endamoeba histolytica* **and other Intestinal Parasites in a Selected Urban Area.** *Amer. J. Trop. Med. & Hyg.* 1954, Nov., v. 3, No. 6, 988–94, 1 fig.

The purpose of this investigation was to determine the prevalence of intestinal parasites in the population of an urban area and compare it with that of an adjacent rural population. Two housing estates with modern sanitary facilities were studied in Memphis, Tennessee, one comprising 429

white families and the other 721 Negro families. The white families had an average period of residence in the estate of 2·8 years and the Negroes 1·3 years. The income of the white families averaged $1,920 per annum and the Negro families $360 less. Volunteers were called for and the sample finally examined consisted of 18 per cent. of each population. Three normal stool specimens were then collected from these at weekly intervals and were examined by direct smear and by concentration methods.

Entamoeba histolytica and *Endolimax nana* were more prevalent in the white population and *Entamoeba coli* among Negroes, but none of the differences was statistically significant. Intestinal amoebae showed their highest incidence in the 15 to 19 age-group and in the case of *E. histolytica* and *E. nana* were more common in women. *Giardia intestinalis* was most prevalent in those under 5 years and in males. The incidence of these parasites was markedly lower than in rural communities in the same area as determined in previous surveys [this *Bulletin*, 1953, v. 50, 1042; 1954, v. 51, 921]. Helminthic infections in the urban population were infrequent, with the exception of *Enterobius vermicularis* which was very prevalent, especially in the white community. There was a significant correlation between a history of diarrhoea and *E. histolytica* infection but none with *E. coli* and *E. nana*. Constipation and abdominal pain were not correlated with any of the parasites. Prevalence of parasites was not related to length of residence in the estates. The findings indicated that in urban conditions transmission occurred mainly in the home and that in rural conditions exposure to parasites was more frequent than in the city and infection took place at an earlier age. *T. H. Davey*

Fassnacht, G. G. & Fooks, J. H. **Engineering Studies on Amebiasis Outbreak at South Bend.** *J. Amer. Water Works Ass.* 1954, Nov., v. 46, No. 11, 1129–40, 2 figs.

At an industrial plant in South Bend (Indiana) cases of infection with *Entamoeba histolytica* were discovered among the workers at the plant in early 1953. A total of 1 to 3 cases per week occurred for a number of weeks and the resulting focus of attention on the disease led to the discovery of cases of this infection in the general community of South Bend. This paper is an account in outline of the engineering studies undertaken in the attempt to trace the source of infection. It gives some particulars of the investigations of a team of workers. A full survey of the plumbing and piping in the drainage and water distribution systems was carried out as well as bacteriological tests of the water and fluorescence tests for possible leakages. The results of the survey are discussed but although the presence of certain defects is recorded, their significance is not definitely stated since "official statements have not yet been released" on the cause of this outbreak of amoebiasis. *M. E. Delafield*

Simitch, T., Petrovitch, Z. & Chibalitch, D. Importance de la coproculture pour la recherche d'*Entamoeba dysenteriae* dans l'amibiase latente et chez les porteurs sains. [**Value of Faecal Cultures for the Detection of** *Entamoeba histolytica* **in latent Infections and in Healthy Carriers**] *Arch. Inst. Pasteur d'Algérie*. 1954, June, v. 32, No. 2, 96–102.

The authors describe the results of a survey for the incidence of infections with *Entamoeba histolytica* among schoolchildren in Yugoslavia. A comparison of the methods of detection of this parasite, by direct microscopical

examination of faecal specimens and by cultivation of this material, convinced them of the superiority of the latter, which is now used in Yugoslavia as a routine method for the diagnosis of amoebiasis. For this purpose, a diphasic medium is used, consisting of Löffler-serum slope covered with saline up to a height of two finger-widths [about 1½ in.] (it is emphasized that poor growth is obtained if the level of the fluid is higher). The person to be examined is invariably purged, and a sample of the stool is diluted in saline before inoculation of 3–5 drops into the culture tube, to which a small amount of rice starch is also added; after this the tube is incubated at 37°C. The cultures are examined 24, 48 and 72 hours later, according to the results. Every time the result is negative, the fluid part of the medium is removed and replaced by fresh saline and starch: it is claimed that this treatment promotes better growth of the amoebae and favours the maintenance of the cultures.

In the course of this work observations were made on the viability of cysts of *E. histolytica* outside the host, which depends on the temperature and humidity of the environment. It was found that cultures could be obtained with cysts from faeces diluted in saline, after preservation in a refrigerator (at −2° to +5°C.) for 7–37 days. However, in parallel specimens kept at 37°C., cultures were successful only after 24–120 hours.

C. A. Hoare

Kasliwal, R. M. **Clinical Manifestations of Amebiasis. An Analysis of 506 Cases.** *Indian J. Med. Sci.* 1954, Nov., v. 8, No. 11, 741–4. [13 refs.]

"Amebiasis with its bizarre clinical picture is quite common in this part of the country as shown by a study of 506 cases of amebiasis in Sawai Man Singh Hospital, Jaipur, from January, 1951, to 30th June, 1953. The cases showed a very varied clinical picture. The commonest symptom complained of by these patients was vague abdominal pain which was poorly localised. A very important physical finding which was observed in nearly 80 per cent of the cases was palpable, enlarged, thickened and slightly tender descending colon and sigmoid colon in the region of left iliac fossa and evidence of slightly palpable liver, which was not tender in a high proportion of cases (nearly 50 per cent). Palpable and enlarged cecum and ascending colon was seen in only 5 per cent of the cases."

Garfinkel, B. T., Alvarez, M. & Oseasohn, R. **The Role of *Endamoeba histolytica* and *Trichuris trichiura* in Bloody Diarrhea of Children in Puerto Rico.** *Amer. J. Trop. Med. & Hyg.* 1954, Nov., v. 3, No. 6, 985–7.

Some children with amoebic dysentery did not show the improvement expected after suitable specific treatment. Sixteen children with a heavy whipworm infection and an *Entamoeba histolytica* infection were suffering from a severe bloody diarrhoea. Some of them were treated with oxytetracycline (1 gm. daily for 10 days); others with enemata of 0·3 per cent. hexylresorcinol in 10 per cent. acacia on three occasions at 3-day intervals; and the rest were kept as controls. The first treatment was anti-amoebic, and the second anthelmintic. The clinical response to the first treatment was negligible, though the amoebae disappeared from the stools. The clinical response to the second treatment was excellent. *A. R. D. Adams*

Payet, M., Pene, P., Rouget-Campana & Barthe, C. Traitement de la dysenterie amibienne par la dibromo-oxyquinoléine (Dibromoquin). [**Treatment of Amoebic Dysentery with Dibromo-Oxyquinoline (Dibromoquin)**] *Bull. Méd. de l'Afrique-Occidentale Française.* 1953, v. 10, 165–8.

This compound is an oxyquinoline compound containing a bromine, and not the more usual iodine, component. Its exact constitution is not stated. The dose recommended is 3 tablets (each containing 250 mgm.) thrice daily, before meals, over a period of 10 days.

Eleven adult Africans suffering from acute amoebic dysentery were treated as indicated. There was a good therapeutic response within 3 or 4 days in 10 cases; symptoms and signs vanished and the parasites had disappeared from the stools. On re-examination 2 to 4 weeks later these 10 patients were still clinically well and stool-negative, and they suffered no toxic side effects from the treatment. The eleventh patient, who was acutely ill with choleraic dysentery, died of uraemia following anuria on the fifth day of treatment with this and other drugs.

In vitro studies of the drug under test show it to have inhibitory action on a culture of amoebae at dilutions of 1 in 20,000 to 1 in 10,000.

A. R. D. Adams

Charmot, G., Le Henand, F. & Giudicelli, P. Traitement de l'amibiase intestinale aiguë en A.O.F. par le Bis (P. arsonophe-nylamino) 1, 2 éthane. [**Treatment of Intestinal Amoebiasis in French West Africa with *bis* (*p.* arsonophenylamino) 1, 2 ethane**] *Bull. Méd. de l'Afrique-Occidentale Française.* 1953, v. 10, 41–3.

In the treatment of intestinal amoebiasis a non-absorbable amoebicide is desirable, as this ensures its greatest concentration in proximity to the causative parasite. This particular compound [4763 RP] has already been studied [this *Bulletin*, 1953, v. 50, 415], and is the subject of the present report by the authors. Twenty Europeans and 11 Africans with intestinal amoebiasis were treated with it at Dakar. The dosage was 2 gm. (4 tablets) of 4763 RP by mouth daily for 10 days; 3 weeks later the course of treatment was repeated. The results are claimed to have been excellent, though of the 18 patients reviewed two months later 2 had suffered relapses.

A. R. D. Adams

Killough, J. H. & Magill, G. B. **A Comparative Study of Fumagillin and Oxytetracycline in Amebiasis.** *Amer. J. Trop. Med. & Hyg.* 1954, Nov., v. 3, No. 6, 999–1007. [12 refs.]

The authors have already recorded some experiences of fumagillin in the treatment of amoebiasis [this *Bulletin*, 1952, v. 49, 696]. Among further male patients in Egypt with microscopically proven *Entamoeba histolytica* infections 67 have been treated with fumagillin and 48 with oxytetracycline [Terramycin]. All were from insanitary surroundings, and suffered from multiple parasitic infections of the bowel. The patients were in hospital and their stools were examined daily while there. The dosage of fumagillin ranged from 5 mgm. to 200 mgm. daily for 14 days; that of oxytetracycline was 2 gm. daily for 10 days to 6 weeks (32 of these latter patients were primarily being treated for *Brucella melitensis* infections). Each group of patients was followed up in hospital for a further 4 weeks; subsequently they were re-examined periodically for a year or two.

Of the 67 patients treated with fumagillin 13 had acute dysentery; 2 of these developed liver abscesses while being treated, and one of them died. Of the 48 treated with oxytetracycline 16 had dysentery; 2 of these developed liver abscesses; another, who probably had an unrecognized abscess before treatment began, died while on oxytetracycline. There were 86 patients (54 on fumagillin and 32 on oxytetracycline) with asymptomatic amoebiasis.

The parasitic response to fumagillin, as judged by stool examinations, was rapid in all but one case; in all but this one case the stools were parasite-free within 3 days. There was symptomatic relief within 9 to 14 days. The parasitic and clinical response to oxytetracycline treatment was similar. Seven of the patients treated with fumagillin had parasitic relapses before leaving hospital. The parasitic relapse rate in both groups in the ensuing months was high, but the significance of this was doubtful as the patients returned to a squalid home environment and might have been reinfected.

The side effects of fumagillin treatment were anorexia, nausea and vomiting; they were transient and not of material significance. A dermatitis involving the face, neck, hands and feet, chest and abdomen appeared irregularly in about one-quarter of the patients.

The general conclusion was that there were no significant differences between the parasitological or the clinical responses to treatment of acute or of asymptomatic amoebiasis with fumagillin and oxytetracycline.

A. R. D. Adams

Self, J. B. **Intraperitoneal Rupture of an Amoebic Abscess of the Liver.** *Postgraduate Med. J.* 1955, Jan., v. 31, No. 351, 35–6.

A case seen in England.

Scaffidi, V. & Li Volsi, M. Sulla terapia delle epatiti colliquative amebiche con clorochina. [**Treatment of Amoebic Liver Abscess with Chloroquine**] *Acta Med. Italica.* 1954, July, v. 9, No. 7, 169–87, 7 graphs & 10 figs. [43 refs.] English summary.

Chloroquine was adopted for the treatment of malaria during World War II, after its schizontocidal properties had been demonstrated in birds. Later, this drug was shown *in vitro* to have amoebicidal properties, and when given to rats it accumulated in their livers in concentrations of as much as 400–500 times the amount which circulated in their blood plasma; hence, in 1948, its adoption for the treatment of amoebic liver abscess.

This paper gives the results of treating 7 patients suffering from amoebic liver abscess with chloroquine; 5 benefited from the treatment. In all but one, the chloroquine represented the first specific treatment: in this case the drug was used in the treatment of a relapse following previous apparent cure of the abscess by emetine. This and another patient were given a " consolidating " course of emetine after what appeared to be successful treatment with chloroquine.

The chloroquine given by mouth led to (a) rapid fall of the pyrexia; (b) early disappearance of the liver symptoms, including the local feeling of distension; (c) gradual reduction of the liver enlargement and of the abscess cavity with lessening of tenderness; (d) rapid general improvement in all cases but one, and, (e) within a varying time, the restoration of the normal blood picture. The drug was well tolerated in aggregate doses of as much as 36 gm. in 20 days. As much as 3 gm. daily have been given over 2 days.

In one of the 2 patients in whom chloroquine treatment failed, the liver abscess burst into the pleural cavity and cure followed emetine treatment. Another patient was taken in hand at quite an early stage of the liver abscess but he failed to obtain any striking benefit from either chloroquine or emetine.

In this series of cases the administration of these specific drugs was combined with tapping of the abscess. *J. Cauchi*

Phillips, B. P. & Bartgis, Ida L. **Effects of Growth** *in vitro* **with Selected Microbial Associates and of Encystation and Excystation, on the Virulence of** *Endamoeba histolytica* **for Guinea Pigs.** *Amer. J. Trop. Med. & Hyg.* 1954, July, v. 3, No. 4, 621–7, 1 fig. [11 refs.]

The dependence of *Entamoeba histolytica* upon associated bacteria and the presence of a bacterial flora of their own in animals used for experimental purposes, represent complicating factors hindering the solution of the mechanism of pathogenesis in amoebiasis. The introduction of bacteria-free cultures of this amoeba, in association with *Trypanosoma cruzi*, at first seemed to have removed one of these obstacles, but it was found that in such cultures *E. histolytica* loses its virulence and is incapable of producing amoebiasis in animals. In the present work, devoted to the elucidation of the factors governing the virulence of this amoeba, attempts were made to exclude these extraneous influences in two ways. First, by using—for intracaecal inoculation of guineapigs—bacteria-free cultures of the associated amoeba + trypanosome at various times following the separation (by antibiotics or micro-isolation) of *E. histolytica* from its concomitant flora. Secondly, by employing in these experiments guineapigs fed on a sterile diet, following the method used at the Lobund Institute, U.S.A., for rearing " germ-free " animals.

These experiments have again shown that a strain of *E. histolytica*, which was highly virulent when accompanied by the original flora, loses its virulence after prolonged culture (21–49 weeks) with the trypanosome alone, though many of the experimental guineapigs harboured amoebae in their gut. However, when inoculated from 1 to 3 weeks after isolation with the trypanosome, bacteria-free cultures produced in guineapigs acute amoebiasis with typical ulceration. But after these cultures were 5 weeks old, their virulence decreased progressively until—at the end of the 8th week—they also became non-invasive. Their virulence could be restored by transferring the amoebae associated with trypanosomes to cultures with bacterial species (*Streptobacillus* and *Clostridium*) and then isolating them again with trypanosomes. Such cultures at first (after 1 week) produced in guineapigs acute symptoms but eventually (after the 7th week) they likewise lost their virulence. Similar results were obtained with cultures of amoebae + trypanosomes derived from amoebic cysts, which had been produced in a culture with a mixed flora after the bacteria-free amoebae associated with *T. cruzi* were returned to it. During the first 2 weeks these cultures were highly virulent, producing acute amoebiasis in guineapigs, but after 6 weeks they lost their virulence for these animals.

It is concluded that these experiments indicate that the accompanying bacteria are not directly involved in the pathogenesis of amoebiasis, but the influence exerted by them upon *E. histolytica* brings about changes in the virulence of the amoeba itself. Furthermore, it is suggested that encystation—induced by contact with bacteria, and therefore absent in bacteria-free cultures—might possibly be the factor promoting the virulence of *E. histolytica*. *C. A. Hoare*

Rees, C. W., Taylor, D. Jane & Reardon, Lucy V. **The Presence of *Endamoeba histolytica* in the Liver of Guinea Pigs with Experimental Intestinal Amebiasis.** *J. Parasitology.* 1954, Aug., v. 40, No. 4, 390–91.

It is now known that guineapigs are highly susceptible to infection with *Entamoeba histolytica*, which produces in the experimentally infected animals a severe intestinal infection with typical ulceration, but hitherto there has been no evidence of the invasion of the liver in these rodents. In order to study this question more thoroughly, slices of liver from infected guineapigs were inoculated into whole egg medium previously seeded with a single bacterial organism known as *t.* In addition to cultures, serial sections of livers from infected animals were examined microscopically for the presence of lesions. Out of 377 cultures 70 (18·6 per cent.) revealed the presence of amoebae, indicating that the livers of 15 of the 20 guineapigs used in these experiments were infected with *E. histolytica.* On the other hand, sections of the livers which were positive in cultures showed no evidence of histopathological changes. In the light of these observations, it is thought that some cases of hepatitis of unknown aetiology in man might be due to amoebic infection of the liver. *C. A. Hoare*

Yoshimura, B. **Experimental Studies on Amoebic Liver Abscess. III. Effects of Associated Bacterial Flora originating from the Same and Different Host Species upon the Production of Experimental Amoebic Liver Abscess.** *Keio J. Med.* Tokyo. 1953, Oct., v. 2, No. 3, 109–17.

With the view to throwing light on the respective rôles played by *Entamoeba histolytica* and the associated bacteria in the production of liver abscesses, the author carried out a number of experimental infections of rats.

In one series of experiments, *E. histolytica* cysts from a human carrier were freed of bacteria, by treating washed cysts with " Homosulfamin " + penicillin + chloramphenicol, and cultivating them in diphasic serum-slant-Ringer medium in two lines: (1) with the original human intestinal flora, and (2) with the intestinal flora of rats. Samples of 0·2 ml. of these amoebic cultures were inoculated directly into the liver of 2 groups of rats: one with the human, the other with the murine flora. The animals were killed after a week and examined for the presence of hepatic lesions and amoebae, in fresh and stained preparations, in serial sections, and by the cultural method. In the group inoculated with bacteria of human origin small liver abscesses were found in over 66 per cent. of the rats, but no amoebae were present; in the group inoculated with the murine flora 43 per cent. showed large abscesses and amoebae were present in 30 per cent. From these experiments it is concluded that the invasiveness of the same strain of *E. histolytica* for the liver depends upon the nature of the associated bacterial flora, the murine one being more favourable than the human one.

The part played by bacteria was brought out more clearly by experiments in which the inoculation into the liver of cultures of *E. histolytica* associated with the murine flora was accompanied by injection of antibiotics (penicillin + streptomycin) into the rats. In these experiments, small liver abscesses were detected in 70 per cent. of the rats but amoebae were absent. It was thus shown that, when freed of bacteria, the amoebae failed to establish themselves in the liver.

In another series of experiments, the amoebae from induced liver abscesses were passaged by serial transfers from liver to culture and back to the liver of new rats, the number of amoebae and size of the lesions increasing with each passage. However, the power of the amoebae to grow in culture diminished progressively until, after the 6th passage, it was completely lost. In order to determine whether this increase of virulence was due to the amoebae or bacteria, a carrier strain of *E. histolytica* which had been cultivated for 18 months and was practically non-invasive for the liver, was inoculated into rat livers together with the flora recovered from the above liver-passages, while control rats were inoculated without this flora. As the result of such treatment, this strain became invasive, producing liver abscesses harbouring amoebae in the majority of the experimental animals, whereas in the controls the abscesses were free of amoebae.

Having demonstrated that the associated bacterial flora plays an important rôle in the production of experimental liver abscess in rats, it is concluded " that in the development of liver abscess in man some intestinal bacteria attain [= reach] the liver with the amoebae through the portal vein and exert their influences on the production of the abscess ". [For parts I and II of this series, see this *Bulletin*, 1954, v. 51, 61, 695.]

C. A. Hoare

Burrows, R. B., Swerdlow, M. A., Frost, J. K. & Leeper, C. K. **Pathology of *Dientamoeba fragilis* Infections of the Appendix.** *Amer. J. Trop. Med. & Hyg.* 1954, Nov., v. 3, No. 6, 1033–9, 15 figs. [16 refs.]

During routine examination of 581 surgically-removed vermiform appendices for intestinal parasites *Dientamoeba fragilis* was found in 4 of them. All 4 patients were whites, and 3 of them were young women. The amoebae were found in the lumina of the appendices, and some (0·6 to 6·8 per cent.) contained engorged red cells; in no case was there evidence of tissue invasion by the parasites. There was marked fibrosis in the walls of all the appendices, and the amoebic infection was thought to be the cause of this.

A. R. D. Adams

McEntegart, M. G. **The Maintenance of Stock Strains of Trichomonads by Freezing.** *J. Hygiene.* 1954, Dec., v. 52, No. 4, 545–50.

" The ability of four species of trichomonads to withstand freezing was investigated with a view to storage of stock cultures. Of the conditions investigated the most satisfactory was found to be storage at −79°C. following slow freezing, the protozoa being suspended in medium containing 10% glycerol. *T. gallinae* was the most easily preserved and survived even without glycerol for 6 months. No observations on survival beyond this period have yet been made, so the possible maximum time of survival is not known.

" *T. vaginalis* remained viable for four months but deteriorated in storage and had died out after 6 months. The sample of *T. hominis* containing 10% glycerol was still viable after 6 months at −79°C., but in the presence of 5% glycerol survival was not observed beyond 4 months. *T. foetus* could not be preserved under any of the conditions tested. The possible implications of these results are discussed."

Simitch, T., Petrovitch, Z. & Lepech, T. Contribution à la connaissance de la biologie des *Trichomonas*.—II. Différenciation de *T. microti* Wenrich et Saxe, 1950 et de *T. intestinalis* Leuckart 1879, par leurs caractères biologiques. [**Biology of** *Trichomonas*. **II. Differentiation of** *T. microti* **and** *T. intestinalis* **by Biological Characters**] *Ann. Parasit. Humaine et Comparée*. 1954, v. 29, No. 3, 199–205.

Trichomonas microti, an intestinal flagellate of the American meadow vole (*Microtus pennsylvanicus*), differs from the human parasite, *T. hominis* —to which the authors refer by its synonym *T. intestinalis*—in having a shorter and thicker body, a shorter flagellum accompanying the undulating membrane and not reaching the posterior end of the body, and only 4 anterior flagella. This flagellate was found in a number of other rodents in America in addition to the vole. The senior author and his associates have previously reported the presence of *T. microti* in mice of Yugoslavia. They now describe investigations carried out with the view to determining the natural and experimental hosts of *T. microti*, and its biological differentiation from the human trichomonad.

For the detection of the infections, caecal contents of the rodents were cultivated at 22–25°C.; if *T. microti* was present, it could be distinguished by the appearance of giant forms dividing by multiple fission. It was found that mice were naturally infected with *T. microti* and susceptible to experimental infection with *T. hominis*, whereas rats harboured the latter but were susceptible to infection with the former. Guineapigs and susliks (*Citellus citellus*) were not naturally infected with either of these trichomonads but they—as well as dogs and cats—were susceptible to experimental infection with both. A human volunteer was proved to be refractory to infection with *T. microti*. Finally, chickens were also refractory to the rodent flagellate but could be infected with the human one.

The authors discuss the affinities between *T. hominis* and *T. microti*, and point out that, while the morphological characters used to distinguish them are inconstant and therefore unreliable, the differences in host-specificity, and the cultural characters, provide sufficient grounds for regarding them as distinct species which can be differentiated biologically by the results of inoculation of chickens. *C. A. Hoare*

Poddar, J. & Chhetri, M. K. **Recent Antimalarials in Giardiasis.** *Indian Med. Gaz.* 1954, Mar., v. 89, No. 3, 155–7.

Of 26 patients in all of whom it is stated that the symptoms were entirely due to infection with *Giardia intestinalis*, 13 were treated with chloroquine (Nivaquine) and 13 with amodiaquine (Camoquin). The dosage of chloroquine used in 7 cases was 2·4 gm. (base) spread over six days, and in the remaining 6 it was 3·1 gm. chloroquine (base) spread over seven days. All those treated with amodiaquine were given a single dose of 600 mgm. (base).

Of the 13 patients treated with chloroquine, 10 complained of side effects which included giddiness, weakness, anorexia and insomnia. Fewer side effects were noted in those treated with amodiaquine.

Clinical improvement followed treatment in all cases but the stools of only 7 of the 13 patients treated with chloroquine became free from parasites within one week of completion of treatment; in the amodiaquine series 8 out of 13 became parasite-free.

The conclusion reached, with which few will disagree, was that for the treatment of giardiasis, chloroquine and amodiaquine do not appear to be superior to mepacrine when given in standard doses. *A. W. Woodruff*

RELAPSING FEVER AND OTHER SPIROCHAETOSES

Hoogstraal, H. **Ticks (Ixodoidea) and their Medical Relations in the Near East.** *J. Egyptian Pub. Health Ass.* 1954, v. 29, Nos. 1/2, 1–8.

This is a useful review of our knowledge of the various ticks of medical importance in the Near East. The rôle of ticks in the transmission of relapsing fever and Q fever in this region has already been studied. However, the bionomics of the vector species and their hosts seem to have been only fragmentarily investigated. The purpose of the present paper is to stimulate interest in a more intensive study of the possible tick vectors of these diseases and of others such as tularaemia, anthrax and the typhus fevers, so that the knowledge already gained in the field and laboratory could be placed on a sounder basis. *M. G. R. Varma*

LEPROSY

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

Short, Eileen I. **The Effect of PAS on the Distribution of Sulphetrone after Simultaneous Administration of the Drugs.** *Brit. J. Pharmacol. & Chemotherapy.* 1954, Sept., v. 9, No. 3, 271–9, 8 figs.

In these investigations sulphetrone was estimated by a modification of the Bratton and Marshall method for sulphonamides. The two drugs were estimated in the presence of each other by determining the total concentration, in terms of sulphetrone, by the diazonium reaction and the amount of PAS by the reaction with p-dimethylaminobenzaldehyde. From this the true concentration of sulphetrone can be calculated (Short, *Biochem. J.*, 1951, v. 48, 301).

Groups of 18 mice were each given 0·625 gm./kgm. doses of the drugs (together or separately) by stomach tube or 0·25 gm./kgm. parenterally. Blood concentrations were estimated from pooled tail blood at 0, ½, 1, 2, 4, 4½ and 6 hours. The simultaneous administration of PAS led to a 3- to 4-fold increase in sulphetrone concentration within half to one hour, after which it fell gradually and at 6 hours differed little from that produced by the same dose of sulphetrone alone. This increase closely paralleled the PAS blood concentrations. Similar results were obtained in rabbits and dogs.

When the drugs were administered parenterally the effect of PAS on sulphetrone blood concentration was still noted, but was less marked. In mice the blood concentration of sulphetrone in the presence of PAS was one and a half to twice that without PAS. In rabbits a 15–30 per cent. and in dogs a 20–40 per cent. increase was obtained.

Urinary and biliary excretion of sulphetrone in rabbits and dogs was increased during the period of increased blood concentration.

It was next shown that *in vitro* sulphetrone and PAS are bound to plasma proteins to about the same extent, namely 87·1 and 85·6 per cent., respectively. When both drugs were present and the concentration of PAS was double that of sulphetrone these figures were reduced to 74·8 per cent. and 81·9 per cent., respectively.

Studies of tissue distribution in mice showed that the concentration of sulphetrone in all tissues was considerably reduced by the simultaneous administration of PAS. It was thus concluded that there is competition between PAS and sulphetrone for a limited number of protein receptors and thus PAS inhibits tissue storage of sulphetrone.

The simultaneous administration of PAS did not inhibit the side effects of sulphetrone on CO_2 combining power of plasma and methaemoglobinaemia, although these were not increased by the increased blood concentrations of sulphetrone. *Mary Barber*

HELMINTHIASIS

In this section abstracts are arranged as far as possible in the following order:—Trematodes (*schistosomes, other flukes*); Cestodes (*Diphyllobothrium, Taenia, Echinococcus, other cestodes*); Nematodes (*Hookworms, Ascaris, Filarial worms, Dracunculus, etc., Trichuris, Enterobius, Trichinella, etc.*).

Sandosham, A. A. **Malaysian Parasites XIV. Worm Infections of some Malayan Aborigines.** *Studies from Inst. Med. Res. Federation of Malaya.* 1953, No. 26, 210–11.

Faecal specimens from 117 Sakai, a group of Malayan Aborigines inhabiting mainly Pahang and Perak, were examined in 1948 for evidence of helminth infections and the following species were noted: hookworm, 49 per cent.; *Ascaris*, 80 per cent.; *Trichuris*, 24 per cent.; *Enterobius*, *Strongyloides*, *Dipylidium caninum* and *Rhabditis hominis* (adults) were each found on one occasion. Eggs of *Heterodera* sp. were also found on one occasion. *J. J. C. Buckley*

Lewert, R. M. & Lee, C. L. **Studies on the Passage of Helminth Larvae through Host Tissues. I. Histochemical Studies on the Extracellular Changes caused by Penetrating Larvae. II. Enzymatic Activity of Larvae** *in vitro* **and** *in vivo*. *J. Infect. Dis.* 1954, July–Aug., v. 95. No. 1, 13–51, 6 pls. (2 coloured). [40 refs.]

Skin-penetrating helminth larvae, after traversing the stratum corneum and the cellular layers of the epidermis, meet the extracellular barriers of the basement membrane and the ground substance of the dermal connective tissue. Similar barriers exist for larvae whose routes of migration involve passage through other epithelia or through connective tissue elsewhere.

In this paper, which is divided into 2 sections, the authors describe their investigations on the passage of a variety of helminth larvae through the tissues of rodent hosts.

I. The first section is primarily a histochemical study of the changes in the acellular elements of the dermal connective tissue of normal animals during penetration by schistosome cercariae and the infective larvae of species of *Strongyloides*, *Ancylostoma*, and *Nippostrongylus*. Observations are also recorded on the passage of various other stages of some of these helminths through certain other tissues, *e.g.*, penetration of snails by schistosome miracidia and the passage of schistosome ova through the liver and intestinal epithelium of rodents. The penetration of the duodenal mucosa by *Trichinella spiralis* larvae and their subsequent entry into the muscles were also studied in rats. As there is evidence that the acellular elements of the connective tissue exist in states of polymerization that vary with age, growth, and other conditions which affect host physiology, the first section of the paper also includes observations on the effect of such factors on the histochemical changes which occur in the skin after penetration by helminth larvae. The histochemical methods used in these investigations include the Hotchkiss periodic acid-leucofuchsin and intravenous Evans blue techniques. A ferrocyanide method, developed by Dr. S. Permutt to demonstrate the presence and relative amount of free extracellular water in connective tissue, is described for the first time.

II. The second section of the article comprises a study of the enzymatic activity of larvae *in vitro* and *in vivo* in relation to the effects of various helminth stages on connective tissue. Living larvae, homogenates and extracts of the infective stages of various nematode and trematode parasites, and extracts of larvae and adults of a non-penetrating nematode, *Rhabditis pellio*, were tested for collagenase, proteolytic activity and "spreading factor". The techniques adopted in this section of the study are described in detail.

It is impossible, in the course of a short review, to deal adequately with this important paper. Except for a preliminary report by the present authors (*J. Parasitol.*, 1951, v. 37, sec. 2, 20) it appears that this is the first detailed account of a histochemical approach, as distinct from cytological investigations, to the study of the effects of penetrating helminth parasites on the acellular elements of connective tissue. The article should be read in full by those interested in histochemical methods and the biochemistry of helminthiases.

The authors' summary is as follows:—

"Histochemical studies have been made of host tissues being traversed by infective helminth larvae, with particular emphasis on the condition of the extracellular glycoprotein of the dermis. The larvae studied include those of *Schistosoma mansoni*, *Schistosomatium douthitti*, *Strongyloides simiae*, *Strongyloides ratti*, *Ancylostoma caninum*, *Nippostrongylus muris* and *Trichinella spiralis*. The results were as follows:

"1. Profound alterations of the extracellular glycoprotein-containing material of the skin, notably the basement membrane and ground substance, accompany penetration by the schistosomes, *Strongyloides* and *Ancylostoma*. Related changes are noted in tissues containing schistosome eggs and in the snail being penetrated by miracidia.

"2. The larval secretions cause a disappearance of the basement membrane at the site of penetration, formation of water-soluble glycoprotein in the dermal ground substance and an increase in free water in the ground substance.

"3. Helminth penetration causes less alteration of acellular substance in aged rats than in young rats and is correspondingly inhibited. It is of interest that in the old animals, the basement membrane is thicker and is presumably more highly polymerized, as is the ground substance.

" 4. In young hypophysectomized animals, there is also a reduction in the degree of glycoprotein alteration with penetration, again correlated with inhibition of penetration. It is considered significant that these animals, like aged rats, have thicker basement membranes and more highly polymerized basement membrane and ground substance.

" 5. Penetration of the skin is inhibited to various degrees in immune animals and in cortisone-treated animals.

" 6. Intravenous antihistamines have no effect on the rate of penetration or on the glycoprotein changes observed histochemically.

" 7. Skin penetration by *N. muris* is not accompanied by the extensive changes in glycoprotein found with the other skin-penetrating forms studied. Its activity does cause an increase in the free water of the ground substance.

" 8. Penetration of tissues by *T. spiralis* is also unaccompanied by immediate changes in host glycoprotein of the type described for other species. However, progressive changes in the glycoprotein capsule that forms about the larvae in muscle are described.

"9. Enzymatic studies of the larvae listed reveal a correlation between the presence of a collagenase-like activity and the ability to cause changes in the glycoprotein of the host. The larvae of *S. mansoni*, *S. douthitti*, *S. simiae*, *S. ratti* and *A. caninum* possess this enzyme or enzyme complex which is capable of releasing dye from azocoll and is also active against a gelatin substrate. Collagenase is not present in larvae of *N. muris*, *T. spiralis* and *Rhabditis pellio* nor in the plagiorchid and strigeid cercariae tested.

" 10. It is the conclusion of the authors that the mechanism of penetration of those parasites which cause changes in the basement membrane and ground substance of the host skin is related to the production of a collagenase-like enzyme. Alterations of the states of organization of the hosts' glycoprotein are reflected in changes in the ability of the parasites to penetrate ".

This paper is supported by excellent photomicrographs and semi-diagrammatic representations of some of the changes which occur during the migration of the various helminths that have been investigated.

R. B. Griffiths

Moore, D. V. & Meleney, H. E. **Comparative Susceptibility of Common Laboratory Animals to Experimental Infection with** *Schistosoma haematobium*. *J. Parasitology*. 1954, Aug., v. 40, No. 4, 392–7.

" In this study, albino mice, Syrian hamsters, albino rats, guinea pigs and rabbits were used. Only the mice and hamsters were found to be susceptible to infection with *S. haematobium*. Using 47 mice exposed percutaneously to 150 cercariae each, a recovery of 5·3 worms per mouse was obtained or 3·5% of the cercariae employed for exposure. In the 65 hamsters exposed percutaneously to 200 cercariae each, a recovery of 33·8 worms per hamster was obtained or 16·9% of the cercariae employed for exposure. Albino rats, guinea pigs and rabbits proved to be either completely or nearly completely refractory to infection with *S. haematobium*.

" In the mice, the worms reached sexual maturity between 12 and 14 weeks after exposure, but more than 50% of the mature worms were found in the liver. In the hamsters, all of the worms reached maturity at 10 weeks after exposure, and a greater proportion of mature worms migrated to the mesenteric veins where eggs which were deposited had an opportunity to be excreted in the feces. In both mice and hamsters, intestinal egg lesions were essentially limited to the ileum and colon. In hamsters, the colonic egg lesions were most numerous in the ascending and

transverse colon, with the greatest concentration of eggs found in the hepatic flexure. Few or no eggs were seen in the descending colon.

" No bladder lesions were seen in any of the mice, indicating that there is no migration of worms from mesenteric to vesicular circulation up to 14 weeks in mice. Only a few hamsters exhibited bladder lesions, the earliest being observed at 14 weeks after exposure, indicating that the migration of worms to the pelvic circulation in hamsters is not consistent, at least up to 20 weeks.

" Viable eggs were first found in the feces of infected mice 15 weeks after exposure. In hamsters viable eggs first appeared in the feces at 10 weeks. Egg passage in the mice seemed to be sporadic, while in the hamster the number of eggs passed increased for several weeks, and began to decline about 20 to 25 weeks after infection. Viable eggs were found in the feces of mice 62 weeks after infection and in hamsters 75 weeks after infection.

" Considering the factors of worm recovery, prepatent period, migration of the mature worms to the mesenteric circulation, and passage of eggs in the feces, the hamster is the most suitable animal of those employed in these experiments."

DE AZEVEDO, J. F. & DE MEDEIROS, Lidia do C. M. L'identification de *Planorbis metidjensis*, Forbes, de l'Algarve (sud du Portugal) d'après la morphologie des organes génitaux et radula; sa comparaison avec les mêmes éléments de *Planorbis corneus*. [**Identification of** *Planorbis metidjensis* **of Algarve, Portugal, by means of the Morphology of the Genitalia and Radula, in comparison with those of** *Planorbis corneus*] *Bull. Soc. Path. Exot.* 1954, v. 47, No. 3, 460–68, 9 figs. (3 on 2 pls.).

In this work the authors set out to investigate the identity of the Planorbid species occurring in Algarve (Southern Portugal) which is an endemic focus of *S. haematobium*. Hitherto it has been regarded as *P. metidjensis* Forbes, having been identified as such on external characters alone. It was thought desirable to examine its internal anatomy, especially the genitalia and radula, and to compare these with those of *P. corneus* as described by BAKER (1945, The Molluscan Family Planorbidae, Urbana). (According to some opinions, *P. corneus* does not occur in Portugal.) From their observations and measurements and the comparison of these with Baker's description of *P. corneus*, the authors conclude " it seems to us that there is no reason to consider the snails from Algarve as a distinct species. Similarly, from our study of the literature concerning the forms from Algarve and North Africa, there is no real reason for considering these forms, either as separate species, as Carlos FRANÇA [this *Bulletin*, 1923, v. 20, 621] wished to do in his monographs of 1922 and 1923 " [abstracter's free translation]. It is intended to confirm this opinion subsequently by comparative studies of the snails in question and of *P. corneus*.

J. J. C. Buckley

TEESDALE, C. **Freshwater Molluscs in the Coast Province of Kenya with Notes on an Indigenous Plant and its Possible Use in the Control of Bilharzia.** *East African Med. J.* 1954, Aug., v. 31, No. 8, 351–65.

In the Coast Province of Kenya schistosomiasis is caused mainly by *S. haematobium*. The few cases of *S. mansoni* which occur are almost always imported. In 3 useful lists of 21 species of fresh-water snails collected in the Province, their distribution, breeding places and habitats

are indicated and the commonest form is *Bulinus* (*Physopsis*) *africanus globosus*, which on circumstantial evidence alone is the vector of *S. haematobium*. Other related species listed are *Bulinus forskali*, *Bulinus corneus*, *Bulinus tropicus* and *Bulinus* (*Ph.*) *nasuta*. [It is unfortunate that *Bulimus putcanus* (?) has been mis-spelt throughout as *Bulinus*, except in Table II.] *Biomphalaria pfeifferi*, vector of *S. mansoni*, is also listed.

The question of control is discussed, with special reference to the use of molluscicides in the form of local plants which are used as fish poisons and contain saponins as the toxic principle. One of these, *Neorautenenia pseudopachyrhizus*, was tested against *B. africanus globosus* in the laboratory and in the field. Five milligrammes of the finely-ground root of this plant killed all snails in 10 cc. of pond water in 24 hours; this dosage being equal to ½ ounce per cubic foot of water. It was non-toxic when given to a monkey to drink for several days. Field tests in two pools (one as control) naturally infested with the snails were carried out at the above dosage and 14 days afterwards there was a considerable reduction in the snail population of the treated pool. "As a molluscicide it has the advantages of being easily applied, costs nothing and is available throughout most parts of the Coast Province; at the tested dose it appears lethal to snails but not to fish and probably does not render the water poisonous to mammals." *J. J. C. Buckley*

Lippi, M. Contributo alla conoscenza dell'appendicite da bilharzia. [**A Case of Schistosomal Appendicitis**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1954, Sept., v. 35, No. 9, 431–8, 1 fig. [24 refs.]

The English summary appended to the paper is as follows:—

"After a brief summary of literature on the subject, the author describes a case of schistosomal appendicitis personally observed in the Yemen."

See also p. 407, Rose, **Peptic Ulceration in Southern Nigeria.**

Payet, M., Pene, P. & Camain, R. Les néphrites bilharziennes. [**Schistosomal Nephritis**] *Bull. Méd. de l'Afrique Occidentale Française.* 1954, v. 11, No. 1, 141–3.

The authors give a brief account of two patients, one a male aged 40 years and the other a female aged 26 years, who suffered from *Schistosoma haematobium* infections with renal involvement and uraemia from which they died. In both cases the right kidney was found on autopsy to be polycystic; the involvement of the kidneys was ascribable to an ascending interstitial nephritis secondary to a schistosomal cystitis.

A. R. D. Adams

Raoult, A., Michel, L. & Diouf, J. Essai d'un nouvel antibilharzien l'AB 5. [**AB 5, a New Anti-Schistosomal Drug**] *Bull. Méd. de l'Afrique Occidentale Française.* 1953, v. 10, 267–302.

AB 5 is stated to be "1 ascorbo-hypophosphito-antimonio tartrate de calcium et de potassium"; the graphic formula is not stated. It is given both intravenously and orally. The dosage intravenously, which rises from 1 mgm./kgm. to 2·5 mgm./kgm. of body weight, is given daily over a 5-day period; concurrently the drug is given orally, the dose for an adult of 40 kgm. being 5 "tablets" at regular intervals each day [the amount contained in a tablet is not stated].

Details are given of 15 patients at Dakar treated along these lines with AB 5; 14 of the patients suffered from *Schistosoma haematobium* infections, and a single patient from *S. mansoni* infection. Owing to the "indocility" of the patients several courses of the treatment were not completed. Although the authors thought the toxic effects of the treatment to be negligible it seems that the patients complained of discomfort in the chest, and of hot flushes, nausea, vomiting, headache and vertigo during or after each injection. The result of the treatment was considered to be good in so far as disappearance of eggs from the urine or the stools and remission of the symptoms were concerned, and this drug is commended as a valuable addition in the therapy of schistosomiasis by virtue of its efficacy in a short course of treatment and of its safety. *A. R. D. Adams*

Deschiens, R. Mécanisme de l'action léthale de *Cypridopsis hartwigi* sur les mollusques vecteurs des bilharzioses. [**Mechanism of the Lethal Action of** *Cypridopsis hartwigi* **on Snail Vectors of Schistosomiasis**] *Bull. Soc. Path. Exot.* 1954, v. 47, No. 3, 399–401, 4 figs. on 2 pls.

The crustacean *Cypridopsis hartwigi* was shown to be harmful to *Planorbis*, *Bulinus* and *Physopsis* in confined bodies of water and also to small aquatic animals such as infusorians, rotifers and insect larvae (*Bull. Soc. Path. Exot.*, 1953, v. 46, 956). The present paper describes the method whereby the snails are killed by the crustaceans. When placed in large numbers with the snails, the *Cypridopsis* approach them like a swarm of bees and attack the soft parts. They can detach mucus and epithelial cells with their appendages, and use these fragments for food. They also try, unsuccessfully, to enter the anal and respiratory openings of the snails. The first reaction of the snails to the attack is to attempt to escape; and this being ineffectual they finally withdraw completely inside the shell. Thus imprisoned they die of starvation in 24 to 48 hours. The mechanical damage done by *Cypridopsis* to the soft parts of the snails is of lesser importance in causing their death. The question of biological control of the snails is discussed and it is concluded that under natural conditions, where many other aquatic animals are present and larger bodies of water are concerned, the effectiveness of the crustaceans in killing the snails would be much reduced. *J. J. C. Buckley*

Floch, H. & Fauran, P. Essais infructueux d'infection expérimentale de *Tropicorbis kuhnianus* (Clessin) par *Schistosoma mansoni*. [**Failure to Infect** *Tropicorbis kühnianus* **experimentally with** *S. mansoni*] *Bull. Soc. Path. Exot.* 1954, v. 47, No. 3, 452–9. [18 refs.]

Although intestinal schistosomiasis is of little importance in French Guiana it occurs in Surinam and in the Antilles. Its introduction therefore depends on the susceptibility of the local snails, which the authors investigated experimentally. They collected snails at Cayenne and its environs and found the commonest species to be *Tropicorbis kühnianus* (Planorbidae). They also found *Stenophysa marmorata* (Physidae) and *Potamopyrgus crystallinus* and *P. coronatus* (Bithyniidae). Dissections of 1,317 *T. kühnianus* and 386 *S. marmorata* revealed no naturally infected snails. The experimental work consisted of exposure on 8 occasions of *Tropicorbis kühnianus* to infection with miracidia of *S. mansoni*. A total of 816 snails were exposed and of them 300 survived. No schistosome cercariae were found in 293 snails dissected, but in 7 there were cercariae with non-bifid tails. These results confirm clinical and parasitological observations that *T. kühnianus* is an unsuitable intermediary. The authors also arrive at

the general conclusion that the importance of other species of *Tropicorbis* known to be potential vectors (*T. centimetralis* and *T. havanensis*) is largely eclipsed by various species of *Australorbis*, especially *A. glabratus*, which are found in the American endemic areas. *J. J. C. Buckley*

Mansour, T. E. & Bueding, E. **The Actions of Antimonials on Glycolytic Enzymes of** *Schistosoma mansoni*. *Brit. J. Pharmacol. & Chemotherapy*. 1954, Dec., v. 9, No. 4, 459–62, 2 figs. [15 refs.]

The effect of certain antimonials on glycolysis by homogenates of *S. mansoni* and on some of their enzymes is described in this communication. Previously Bueding has shown [this *Bulletin*, 1951, v. 48, 653] that glycolysis, which appears to be more necessary for the survival of the intact worm than respiration, is in their case affected by these compounds. The techniques for obtaining the adult worms were as described by the authors [*ibid.*, 1954, v. 51, 407]. The worms were then homogenized in glycylglycine buffer at a final *p*H concentration of 7·5 in a suitable medium, whose composition is described. The substrates were glucose, fructose-6-phosphate and fructose-1:6-diphosphate and the amount of glycolysis was measured by the lactic acid formed after shaking at 38°C. for 1 hour.

When glucose was the substrate the trivalent antimonials, Stibophen and antimony potassium tartrate (tartar emetic), caused marked inhibition of glycolysis. Experiment showed that neither hexokinase nor phosphohexose-isomerase, both of which are concerned with the first two steps in glycolysis, was the enzyme involved. Fructose-6-phosphate and fructose-1:6-diphosphate were then used as substrates. Only in the case of the former was lactic acid production affected by the antimonials, indicating that the step whereby it is converted to fructose-1:6-diphosphate by phosphofructokinase is vulnerable. Whether this interference is responsible for the chemotherapeutic action of the drug is not known. A pentavalent antimonial (sodium stibogluconate) at high concentration had no effect on the activity of the worm enzyme. These results agree with the observation of others [this *Bulletin*, 1936, v. 33, 97] that schistosomes are unaffected by pentavalent antimonials *in vitro*, and suggest that activity follows reduction by the host tissues.

The authors point out that the schistosome hexokinases are affected by trivalent arsenicals in low concentration and therefore the mechanisms of action of the metal derivatives of arsenic and antimony are probably different. Whereas both arsenicals and antimonials act against leishmaniae and trypanosomes, only the latter are effective in schistosomiasis. On the other hand it is known that the hexokinase of *T. equiperdum* is inhibited by low concentrations of antimonials [Chen, *ibid.*, 1948, v. 45, 773]. It appears that the enzyme which catalyses the same reaction in different species may differ in susceptibility to the same inhibitors. *J. D. Fulton*

Dobrovolny, C. G. & Barbosa, F. S. **Field Trials of Sodium Pentachlorophenate as a Molluscacide in Flowing Waters in Brazil.** *Publicações Avuls. Inst. Aggeu Magalhães*. Recife, Brazil. 1953, v. 2, 121–57, 6 figs. [18 refs.]

This account is a preliminary paper on field tests with sodium pentachlorophenate against *S. mansoni vectors*, *Australorbis glabratus* and *Tropicorbis centimetralis* in Pernambuco. These snails prefer the slower and shallower streams in the region and are rarely found in large streams. They are most frequent near villages and towns but the two species are rarely found together in the same waters. The molluscicide, containing about 75

to 79 per cent. active ingredient, was applied to the water as 1 oz. briquettes suspended in muslin bags or on a copper screen, or the " drip method " was employed. Standing waters were hand-treated, or sprayed with dust, or water-sprayed. The rate and content of dispersion of the compound were determined by sampling at different points and pre- and post-treatment snail surveys were carried out. Sixty-three stream units, varying in length from 100 to 3,900 feet, were treated with various concentrations for varying durations and the percentage reduction of the snail populations was observed at subsequent periods of 3 days, 7 days and monthly thereafter for 6 months, and again after 12 months.

" A single application of sodium pentachlorophenate did not eradicate entire snail populations from all streams, but a 100 per cent reduction in the snail population was noted in some streams for periods up to 12 months where the chemical was applied in the more effective ways. For a 4-month period following treatment, a snail reduction of 90 per cent or more was noted in about 40 per cent of the streams examined on each survey. In some entire streams and parts of other streams effective control of the snails was observed for more than 12 months after application of the compound.

" Control of snail population was successful in streams where the chemical was applied at selected intervals of time over periods up to one year. It would appear that in this locality some streams may require 3 or more treatments each at spaced intervals of 3 to 4 months.

" Usually the chemical was most effective in the streams where the largest dosage was applied for the longest period of hours. However, it was observed that concentrations as low as 2 ppm maintained for 40 hours were frequently as effective as high concentrations for shorter periods."

[This paper contains much useful detailed information which is difficult to summarize and it should be consulted in the original by those interested.]

J. J. C. Buckley

Lalouel, J. Bilharziose intestinale à *Schistosoma intercalatum* à Libreville. [**Intestinal Schistosomiasis due to *Schistosoma intercalatum* at Libreville**] *Bull. Soc. Path. Exot.* 1954, v. 47, No. 4, 531–4.

This paper is another reminder that scattered and limited foci of human intestinal infection with *S. intercalatum* exist in tropical Africa. Clapier [this *Bulletin*, 1924, v. 21, 198] first recorded cases from Libreville in 1923, and in the same year the reviewer [*ibid.*, 1923, v. 20, 939] reported the existence of a focus near Stanleyville in the Belgian Congo.

The endemic area is described as " at the back of the hospital " at Libreville. It provided most of the 30 cases diagnosed in 1953. Symptoms, as usual, were mild, and invasion of the urinary tract was never found. Anthiomaline injections banished ova from the stools in 1 to 3 weeks, but no effort was made to evaluate the permanence of " cure ".

A search in the swampy lakes of the area revealed none of the recognized vectors, though single-tailed cercariae were found in most of the *Lymnaea*, the predominant mollusc there.

C. C. Chesterman

DeWitt, W. B. **Susceptibility of Snail Vectors to Geographic Strains of *Schistosoma japonicum*.** *J. Parasitology.* 1954, Aug., v. 40, No. 4, 453–6, 1 fig. [10 refs.]

" In this study, laboratory-reared *Oncomelania hupensis* originating from Shanghai, China; *O. nosophora* from Kofu, Japan; *O. formosana* from Chang Hua, Formosa; *O. quadrasi* from Leyte and Mindanao, P.I.; and

Pomatiopsis lapidaria from the Potomac River near Washington, D.C. were exposed to strains of *Schistosoma japonicum* from Shanghai, China; Kofu, Japan; and Chang Hua, Formosa. *O. hupensis* was readily infected with the Chinese and Japanese strains but in these tests could not be infected with the Formosan strain. *O. nosophora* was susceptible to both the Japanese and Formosan strains but was refractory to the Chinese strain. *O. formosana* became infected with the Formosan strain but could not be infected with the Chinese and Japanese strains. *O. quadrasi* was susceptible only to the Formosan strain while *P. lapidaria* was infected with the Chinese and Formosan strains but not the Japanese strain." [These results are clearly illustrated in a simple diagram.]

Sawada, T., Suzuki, I., Oka, T. & Sano, M. **Studies on the Diagnosis of Schistosomiasis japonica.** *Gunma J. Med. Sci.* Maebashi. 1954, Jan., v. 3, No. 1, 39–47, 1 diagram. [11 refs.]

"Conclusions which may be drawn from these studies are as follows:

"The watersoluble protein fraction which is obtained from adult *S. japonicum* worms by half saturated ammonium sulfate is more sensitive than the watersoluble polysaccharide fraction. It is considered that the diagnostic method which has been employed to find eggs of *S. japonicum* in the stools of patients is not practical and unreliable, but if the dermal test is improved and suitable antigen is produced, the existing trouble will be eliminated."

de Meillon, B. & Stoffberg, N. **"Swimmer's Itch" in South Africa.** *South African Med. J.* 1954, Dec. 11, v. 28, No. 50, 1062–4, 1 fig.

The authors report on what they consider to be the first case in Africa of "swimmer's itch", which is caused by the penetration into human skin of cercariae which cannot develop into mature flukes in man. The authors suggest that, now that it is known that "swimmer's itch" occurs in Africa, it may be found to be fairly common there. Cort [this *Bulletin*, 1951, v. 48, 482] has reviewed its incidence in the United States, Canada, Europe, Asia, Australia and New Zealand.

The patient described was a small boy aged 10, who, after bathing in a swampy pool near Johannesburg, developed a severe rash. The rash, accompanied by severe itching, persisted for about 3 days and then subsided. No other symptoms were reported. The area in which the boy bathed is known to be free from human schistosomiasis and the authors' surveys have shown that none of the accepted vectors of *Schistosoma haematobium* or *S. mansoni* occurred in the area.

Each of several visits by the authors to the pool yielded hundreds of *Lymnaea natalensis* and *Bulinus tropicus*, which were shedding at least 6 different types of cercaria. Among them were 4 fork-tailed types, none of which caused dermatitis when they were applied to the skin of monkeys, although further work is being done with them. One of them, however, closely resembled the eye-spotted larvae of *Trichobilharzia ocellata*, a well-known cause of "swimmer's itch", and the authors tested these on 3 human volunteers.

In the first volunteer, who had already been sensitized by previous skin-penetration, itching began 20 minutes after application of the cercariae in water to the arm and, 5 hours later, small red spots appeared, of which a photograph is presented. The itching and redness disappeared 10 days

after exposure to the cercariae, but a month later small discoloured spots were evident.

In the second volunteer application of the cercariae in water produced no reaction, but next day they were applied in a tube inverted over the arm and 15 minutes later itching began and small red spots appeared after 1 hour. The next day itching had gone, but the spots were unchanged; they did not develop, but faded away during the following week. This is interpreted by the authors as a mild reaction in a patient exposed for the first time.

In the third volunteer, who had had " some slight previous exposure ", the reaction was intermediate between those just described. Itching began in about 1½ hours and faint red spots appeared, but 3 hours later the itching disappeared without recurrence, although the red spots became enlarged, raised and nearly colourless weals, which itched intensely for a short time; they disappeared the next day, but left small, slightly-discoloured spots.

Cort (*loc. cit.*) has reviewed the problem of " swimmer's itch " and Hammerli (*Dermatologica*, 1953, v. 107, 302) has published photographs of sections removed by biopsy showing the absorption of the cercariae, which cannot, except very rarely, develop into flukes in man. Variations in the reactions of different people may be due to their variable susceptibility or to sensitization, which may last for years and is not necessarily specific because Olivier [this *Bulletin*, 1949, v. 46, 849] has described severe skin-reactions after penetration by another species of cercaria. Yet increased exposure does not cause, in some people, increased sensitization. Cort (*loc. cit.*) has described the most severe form of " swimmer's itch ", called *koganbyo* in Japan, in which urticarial lesions, severe itching, loss of sleep and sloughing of the skin develop and the body and face may swell up and the axillary and inguinal glands enlarge, the patient often having to go to bed for some days. So far as *Schistosoma haematobium* and *S. mansoni* are concerned, Barlow [*ibid.*, 1937, v. 34, 392] has shown that, in persons already infected with these flukes, re-exposure to their cercariae did cause dermatitis, but the present authors repeatedly exposed monkeys to either *S. bovis* or *S. mansoni* without noting itching or dermatitis. The authors suggest that sensitization is linked with immunization. The cercariae of " swimmer's itch " and schistosomiasis both penetrate the skin at the first exposure, the former perhaps being killed off in the lungs or elsewhere and the latter developing into mature flukes. After 1 or 2 exposures some immunity is developed, which makes it difficult for the cercariae to penetrate beyond the epidermis, but the lytic and protein substances that they produce cause the dermatitis observed. Further experimental work on the life history of the cercariae that caused the dermatitis described above and on the " bilharzia complement-fixation reaction, eosinophilia and liver function " is proceeding. *G. Lapage*

Sandosham, A. A. **Malaysian Parasites XII. Cercarial Dermatitis caused by a Member of the " Elvae " Group.** *Studies from Inst. Med. Res. Federation of Malaya.* 1953, No. 26, 195–8, 1 fig. [13 refs.]

In 1948 the skin condition known locally as " sawah itch " [this *Bulletin*, 1939, v. 36, 40] was unusually severe in a district of Negri Sembilan in Malaya. The author examined 72 snails (*Lymnaea crosseana*) from the area and found furcocercous cercariae in 13 of them. The cercariae caused a pricking sensation when placed on the forearm and after 3 hours the skin became slightly raised and somewhat inflamed. Two chickens were exposed to infection with the cercariae but no adult infection resulted.

The morphology and behaviour of the cercariae are described; they are referred to the " Elvae group " and are thought to be larval forms of some member of the Bilharziellinae, possibly *Trichobilharzia*, and are provisionally named *Cercaria malayi* I. The author discusses the probability that allergy may take part in causing " sawah itch " in Malaya. *J. J. C. Buckley*

Kendall, S. B. **Fascioliasis in Pakistan.** *Ann. Trop. Med. & Parasit.* 1954, Sept., v. 48, No. 3, 307–13, 4 figs. on pl. & 1 map. [22 refs.]

" In Pakistan, the two species of fluke *Fasciola hepatica* and *F. gigantica* are transmitted respectively by the two snails *Limnaea truncatula* and *L. auricularia rufescens*, which differ markedly in their ecological requirements and in their geographical distribution. It is suggested that throughout the world all the snail hosts of *F. hepatica* and all the snail hosts of *F. gigantica* are likely to correspond respectively, both in form and in ecology, with the snails *L. truncatula* and *L. auricularia* sens. lat."

Ramanujachari, G. & Alwar, V. S. *Paryphostomum sufrartyfex* **(Lane, 1915) Bhalerao, 1931 in Pigs** (*Sus scrofa domestica*) **in Madras.** Reprinted from *Indian Vet. J.* 1954, May, v. 30, No. 6, 498–500.

Paryphostomum sufrartyfex (Lane, 1915) was found in 2 out of 54 pigs examined in Madras. This is the first time it has been recovered from pigs in Madras. Only 6 specimens were collected and from these eggs were obtained and cultured in tap water. Most of the eggs hatched 11 days later and *Lymnaca lutcola* and *Indoplanorbis exustus* were exposed to the miracidia but all the snails died after about 2 days. It is thought however that *L. lutcola* are the first intermediate host and that common fishes such as *Barbus stigma*, and also snails, are second intermediate hosts.

J. J. C. Buckley

Lumme, R., Mustakallio, K. K., Telkkä, A. & Tötterman, G. **Uropepsin Excretion in Pernicious Tapeworm Anemia.** *Acta Med. Scandinavica.* 1954, Nov. 30, v. 150, No. 4, 321–5. [14 refs.]

The authors quote the statement by Bucher (*Gastroenterology*, 1947, v. 8, 627) that uropepsin, a proteolytic enzyme, is derived from the gastric peptic cells as a pepsinogen, most of which is secreted into the lumen of the stomach, where it is converted, in the presence of HC1, into pepsin, the remainder being passed into the blood to be excreted in the urine as uropepsin, the determination of which in the urine provides evidence of the function of the peptic cells. Spiro *et al.* (*J. Lab. & Clin Med.*, 1950, v. 35, 899) showed that its secretion is controlled by the adrenal cortex. The authors also quote literature which reports that, in Addisonian pernicious anaemia, uropepsin is either absent from the urine or is excreted only in minimal amounts. They themselves have studied the excretion of uropepsin in pernicious tapeworm anaemia caused by *Diphyllobothrium latum* and have compared the results obtained with results of studies of patients suffering from Addisonian pernicious anaemia.

In all, 45 patients with pernicious tapeworm anaemia (18 men, 27 women) and 17 patients with Addisonian pernicious anaemia (4 men, 13 women) were studied. The insulin test for gastric secretion was done on 31 cases of pernicious tapeworm anaemia and on 14 cases of Addisonian pernicious anaemia. Determinations of haemoglobin, erythrocytes, leucocytes and reticulocytes were done by routine methods and 53 cases were

diagnosed without bone-marrow examinations. In 9 cases the diagnosis was confirmed by bone-marrow examinations. Diagnosis of pernicious tapeworm anaemia was based on the presence of tapeworm eggs in the faeces, on the blood picture and on the improvement in this when the tapeworm was expelled. Uropepsin determinations were done by the method of West *et al.* (*J. Lab. & Clin. Med.*, 1952, v. 39, 159) with urine collected over 24 hours. The normal range for uropepsin excretion was 10–50 units per hour.

Tables summarize the results. In 14 cases of pernicious tapeworm anaemia the uropepsin excretion was also determined 5–10 days after expulsion of the tapeworm. In 4 of these cases there was a significant increase in the uropepsin excretion, in 3 a slight increase and in the other 7 no substantial alteration. In patients with Addisonian pernicious anaemia the administration of liver, vitamin B12, intrinsic factor, pepsin or corticotrophin did not alter the rate of uropepsin excretion.

The authors conclude that 50 per cent. of patients with pernicious tapeworm anaemia showed a normal rate of uropepsin excretion, if 10 units per hour is taken as the lowest normal value. The excretion was subnormal in 20 per cent. of patients aged 50 and in 65 per cent. aged over 50, so that age seems to affect the rate of excretion. In about 75 per cent. of patients with pernicious tapeworm anaemia presence of free HCl in the stomach was associated with normal uropepsin values; and the absence of free HCl was associated with subnormal uropepsin values. But one-third of the patients who were unable to secrete free HCl showed normal uropepsin excretion. Only 2 patients showed subnormal uropepsin excretion without achlorhydria. Normal uropepsin excretion is much commoner in patients with pernicious tapeworm anaemia than in those with Addisonian pernicious anaemia, only one of the latter showing normal uropepsin excretion. The authors quote evidence indicating that the functional capacity of the gastric mucosa is higher in patients with pernicious tapeworm anaemia than in those with Addisonian pernicious anaemia and that ability to secrete HCl can reappear after expulsion of the tapeworm. The determination of uropepsin seems to be more valuable than the insulin test for free HCl and is more pleasant for the patient. In pernicious tapeworm anaemia the uropepsin excretion was not correlated with the reticulocyte response after expulsion of the tapeworm, nor did the severity of the tapeworm anaemia influence the rate of excretion of uropepsin. *G. Lapage*

Rafaelsen, O. J. Taeniasis behandlet med mepacrin. [**Taeniasis treated with Mepacrine**] *Ugeskr. f. Laeger.* 1955, Jan. 13, v. 117, 54–6. [14 refs.] English summary.

In a Danish hospital Rafaelsen has treated 20 cases of *Taenia* infection with mepacrine (atebrin or quinacrine), which he has found in many respects preferable to *Filix mas* as a vermifuge. During the first two days in hospital the patients were given a low-residue diet and laxatives as well as an enema. On the morning of the third day 800 mgm. of mepacrine were given by mouth with a little milk or water, followed by laxatives and an enema. If by next day the scolex had not appeared, the treatment was repeated. In 16 of the 20 cases the scolex was found, and in the remaining 4 cases many mepacrine-stained segments were evacuated at the time, but not later. The first two patients were given mepacrine through a duodenal tube, but this precaution was subsequently regarded as superfluous. The preliminary treatment for 2 days with laxatives was kept up as it facilitated the finding of the scolex, and but for this consideration may perhaps have been superfluous. It is also doubtful if the administration of a laxative on

the day of treatment, as recommended by many, is absolutely necessary. Most of the patients experienced a moderate degree of nausea, and one or two vomited, but in every case the discomforts provoked by the treatment had passed off on the day of the cure. Patients with experience of *Filix mas* declared that the discomforts of mepacrine treatment were certainly less troublesome. *Claude Lillingston*

Simitch, T. & Keckarovska, J. Infestation de *Citellus citellus* par *Hymenolepis nana* à partir de cysticercoïdes et de parasites adultes. [**Infection of *Citellus citellus* with *Hymenolepis nana* by Means of Cysticercoids and Adult Parasites**] *Arch. Inst. Pasteur d'Algérie.* 1954, June, v. 32, No. 2, 103–6.

With *Citellus citellus* as experimental animals, 3 series of experiments were carried out with *Hymenolepis nana*. In the first of these, 12 adult *C. citellus* were given orally cysticercoids of ages from 1 to 6 days. From 4 of the animals 45 adult *H. nana* were recovered. In the second series, 12 young *C. citellus* were given cysticercoids 1 to 2 days old and from 4 of the 12, 24 *H. nana* were recovered. In the third series, 6 *C. citellus* were given the scolices and anterior parts of the strobila of *H. nana*. They were all autopsied 15 days later and only 4 *H. nana* were recovered.
J. J. C. Buckley

Walshe, J. M. **Echinococcosis Alveolaris of the Liver.** *J. Path. & Bact.* 1954, Apr., v. 67, No. 2, 371–7, 3 figs. on pl.

The author gives an account of echinococcosis alveolaris in the liver of a woman of 45, apparently the first case of this kind to be recorded in Great Britain. The patient had symptoms of lassitude from 1947 to 1950 when a medical examination revealed marked enlargement of the right lobe of the liver. Hospital investigation " showed a normal blood count and blood urea and a negative Wassermann reaction. At laparotomy she was found to have a single, large, hard white mass in the right lobe of the liver. It had the appearance of secondary carcinoma, but no primary growth could be found elsewhere. A biopsy was taken and was thought to show a degenerating hepatoma ". After 2 years of deterioration, remarkable improvement occurred. She was admitted to University College Hospital, London, in November 1952, for further investigation, and the liver biopsy section of 1950 was re-examined—as it was felt that the diagnosis had to be revised—and found to have the typical appearance of echinococcosis alveolaris. Casoni tests were negative but complement-fixation tests were positive. Severe haematemeses occurred early in 1953 which necessitated blood transfusion and the patient died after a further haematemesis in May 1953. On post-mortem examination the cause of death was found to be haemorrhage from oesophageal varices and liver failure. The liver weighed 4,300 gm., the left lobe being hypertrophied and showing well-developed diffuse hepatic fibrosis while the right lobe contained a cavity 10 cm. in diameter with a ragged, necrotic wall and was filled with turbid, bile-stained fluid in which no scolices or hooklets were found. The liver tissue was densely necrotic and contained multiple cystic spaces up to 0·5 cm. in diameter. Histological examination of the lesion in the right lobe showed the presence of a single scolex.

This interesting case is discussed at length by the author with special reference to the aetiology of echinococcosis alveolaris and the question of the possible duality in form of the adult worm, *Echinococcus granulosus*; he rejects the dualist theory. He is also of the opinion that the diffuse

hepatic fibrosis associated with the infection is "a direct result of the parasitic invasion of the liver and not a preceding abnormality which itself gives rise to the larval variation". *J. J. C. Buckley*

Dollfus, R. P. & Canet, J. Sur un Pentastomide: *Raillietiella* (*Heymonsia*) *hemidactyli* M.L. Hett 1934. Supposé susceptible de parasiter l'homme consécutivement à l'ingestion thérapeutique de lézards vivants. [**Suspected Parasitism in Man by a Pentastome** *Raillietiella* (*H.*) *hemidactyli* **after "Therapeutic" Ingestion of Lizards**] *Bull. Soc. Path. Exot.* 1954, v. 47, No. 3, 401–7, 6 figs.

On three occasions in Indo-China general and cutaneous symptoms resembling "creeping disease" were observed by one of the authors in 3 Vietnamese people, all of whom had in the previous weeks eaten 5 to 10 living geckonid lizards, locally known as *margouillats*. This practice of eating live geckoes is due to the local charlatan doctors who prescribe them for people suffering from bronchial asthma, emphysema and cervical fistulous tuberculous adenitis. The "dosage" may be 2 to 6 lizards per day, sometimes over a period of several weeks.

The skin condition in the 3 cases was treated with local freezing. No parasites were found in the blood but there was eosinophilia of 15 to 30 per cent. In the belief that the skin condition might be due to a parasite, possibly a parasite of geckoes, the authors examined 50 of these lizards and in the lungs of 14 of them (28 per cent.) found 1 to 8 specimens of *Raillietiella* (*Heymonsia*) *hemidactyli* Hett, 1934, a pentastomid parasite which has not hitherto been recorded from lizards in Indo-China. The lizards found infected belonged to 2 species, *Hemidactylus frenatus* and *Gehyra mutilata*.

The parasite is illustrated and described and its life-cycle (of which little is known) is discussed. It is thought possible that the skin condition is a pseudo-myiasis caused by the larvae of *R.* (*H.*) *hemidactyli* which have gained access to the human host after the latter has ingested lizards infected with the adult parasites in the lungs. This supposition can only be proved by demonstrating the larvae in the subcutaneous channels and abscesses which have appeared after the ingestion of infected lizards.

J. J. C. Buckley

Mauzé, J. Un cas d'ankylostomiase du nourrisson. [**A Case of Ankylostomiasis in an Infant**] *Bull. Soc. Path. Exot.* 1954, v. 47, No. 3, 411–12.

A case in Guadeloupe in an infant on a wholly milk diet.

Sawada, T., Suzuki, I., Oka, T. & Sano, M. **Diagnosis of Ancylostomiasis by means of Intradermal and Serological Tests.** *Gunma J. Med. Sci.* Maebashi. 1954, Jan., v. 3, No. 1, 29–38, 1 diagram. [12 refs.]

"(1) Precipitin tests and Middlebrook-Dubos haemagglutination tests were conducted and the results thereof were described did not serve satisfactory.

"(2) Protein and Polysaccharide fractions were prepared from the adult *Ancylostoma caninum* and tested in dogs and men.

"(3) Protein fractions used as test antigens showed fairly satisfying results.

"(4) Polysaccharide fraction used as a test antigen showed unsatisfactory results."

André, L. M., Lamy, L. & Agboton, D. Alimentation supplémentaire par le lait écrémé. Ankylostomose et gains pondéraux chez l'enfant africain. [**Supplementary Feeding with Skimmed Milk. Ankylostomiasis and Weight Gain in African Children**] *Bull. Soc. Path. Exot.* 1954, v. 47, No. 4, 535–9.

This paper sets out to compare the value of giving supplementary protein in the form of skimmed milk and of removing the parasites, both separately and together, in the treatment of ankylostomiasis. Studies of the weight gain after treatment showed that much the best results were generally obtained in children who were wormed after a preliminary period of supplementary feeding. The amount of dried skimmed milk powder given was usually 40 gm. a day, reconstituted with a quarter of a litre of water.

R. Passmore

Sawada, T., Sano, M. & Ueno, T. **Studies on the Development of *Ancylostoma* Larvae in Chicken Embryo.** *Gunma J. Med. Sci.* Maebashi. 1954, Jan., v. 3, No. 1, 21–8, 18 figs. [13 refs.]

The authors cultured to the infective larval stage the eggs of *Ancylostoma duodenale* and *A. caninum*. The larvae were measured and about 100, treated either with serum (human or canine) or lung infusion, were injected into the yolk sac (6 days later) or allantois (10 days later) of chicken embryos. After varying intervals the growth of the larvae was determined. It was found that some of the larvae of *A. caninum* remained alive in the yolk sac and the allantois for 6 to 10 days. In general there was a slight increase in length and breadth and some internal change but there was no development of the provisional buccal capsule in larvae injected into the yolk sac. In larvae injected into the allantois the provisional buccal capsule developed.

The larvae of *A. duodenale* increased in size and development rather more than those of *A. caninum*, especially in the allantois, in which 10 days after injection there was not only development of the buccal capsule but the sex of the larvae could be determined.

J. J. C. Buckley

Ritchie, E. B. & King, W. C. **Observations on the Reactions of the Larvae of *Ancylostoma caninum* and *Ancylostoma braziliense* to Various Drugs and Chemical Compounds based on *in vitro* Tests.** *J. Investigative Dermat.* 1953, May, v. 20, No. 5, 337–41.

In the region of the Gulf of Mexico, the treatment of creeping eruption due to these larvae is still unsatisfactory. Treatment with ethyl chloride spray is painful and tedious, and Fouadin and diethylcarbamazine have been disappointing.

In the authors' experiments, larvae were obtained by culture from the faeces of a cat. The filariform larvae were placed in water (1 drop) in welled slides 3 mm. deep, and the chemical (2 drops) was added. [Therefore the chemical was diluted to two-thirds of its normal concentration.] The larvae were watched through a microscope at room temperature for 3 hours; 30 per cent. of the controls died during this time probably owing to the light and heat. With 6·3 per cent. Fouadin and 2·5 per cent. diethylcarbamazine [presumably the citrate which is acid] 10 per cent. of the larvae survived for 24 hours. Among the compounds which exerted complete larvicidal action in 5 minutes were:—acetone, ethyl acetate, ethyl formate, pyridine and 95 per cent. ethyl alcohol; among those completely larvicidal within 30 minutes were ammonium chloride, and sulphate, sodium

chloride, and sucrose (saturated concentrations). Hexylresorcinol 0·06 per cent. in water, killed in less than 90 minutes; and Stibanose 2·0 per cent. in less than 3 hours. Action was incomplete after 3 hours with oxytetracycline 10 per cent., aureomycin 10 per cent. and several other antibiotics. Action was incomplete after 24 hours with oxophenarsine 0·6 per cent., mepacrine 1·0, suramin 1·0 per cent., and various other compounds.

F. Hawking

Pan, C., Ritchie, L. S. & Hunter, G. W. **Reinfection and Seasonal Fluctuations of *Ascaris lumbricoides* among a Group of Children in an Area where Night Soil is used.** *J. Parasitology.* 1954, Oct., v. 40, No. 5, Sect. 1, 603–8, 1 fig. [24 refs.]

"Reinfection with *A. lumbricoides*, following treatment, has been investigated in Japan where night soil is extensively used in vegetable gardens. Monthly examinations were made on a group of teen-age children over a period of 14 months. Within 2 months after treatment reinfections began to appear, approaching the original incidence and intensity of infection after 1 year. A sharp decline in the level of both incidence and the parasite-density index of *Ascaris* occurred in September. Maximum levels of infection existed during the winter and summer months, between which a record decline in the spring may have occurred. Possible explanations for these seasonal fluctuations are based upon the combined effect of seasonal variations in diet and time of applying night soil. The findings confirm a relatively short life span for *Ascaris lumbricoides*."

Pfister, R. Résultats d'une enquête sur les porteurs de microfilaire en Afrique Occidentale Française. [**Survey of Carriers of Microfilariae in French West Africa**] *Bull. Soc. Path. Exot.* 1954, v. 47, No. 3, 408–11.

The author's summary in French is translated freely as follows:—

From each of 10,169 apparently healthy Africans we have examined a single drop of blood and a single drop of fluid from skin scarification and observed parasites in 40 per cent.: namely *D. perstans* 31 per cent., *O. volvulus* 5·7 per cent., *W. bancrofti* 3·8 per cent., *D. streptocerca* 0·1 per cent.

Away from the desert regions of the Sahara and to the south one first finds *W. bancrofti* almost exclusively, then further to the south *D. perstans*, while *D. streptocerca* is confined to the humid savanna and forests. *O. volvulus* occurs in all zones but especially in the savanna adjoining river courses. The people of the forests are very lightly infected, but those of the savanna often harbour one or several species of filariid worms, apparently with no ill-effects.

J. J. C. Buckley

Chernin, E. **Problems in Tropical Public Health among Workers at a Jute Mill near Calcutta. VI. The Prevalence of Filariasis in the Labour Force with a Note on its Transmission.** *Indian J. Malariology.* 1954, June, v. 8, No. 2, 77–83.

This is the sixth of a series of parasitological investigations carried out among the employees of the Ludlow Jute Company on the Hooghly River some 17 miles south of Calcutta [this *Bulletin*, 1954, v. 51, 644, 828, 829]. Thick smears of about 12 to 15 cmm. of blood were made from 571 volunteers between 9.30 and 11.30 p.m., and 6·8 per cent. were found to contain microfilariae. The corrected infection rate for the whole labour force was

5·5 per cent., which is just over half the incidence in Calcutta. Only one among 87 women was found positive. On analysing the results according to place of origin the most heavily infected group (15 per cent.) came from Uttar Pradesh, but was one of the smallest. The largest provincial group came from Orissa and this was next most heavily infected (10·4 per cent.). Infections were rare or absent in age-groups below 20 and over 50, and the highest incidence was between 40 and 50. Microfilaraemia was light in over 60 per cent. and only some 4 per cent. had counts of 100 or more microfilariae per thick film. All infections were due to *Wuchereria bancrofti* except one male Oriya who suffered from *W. malayi*. Physical examination of 37 of the 45 infected persons revealed hydrocele in 5, epididymitis in 6 and chyluria in 1. No routine studies were made of possible vectors, but of 97 *Culex fatigans* dissected 2 proved to be infected. The disease, though not of great importance among the mill workers, probably causes some morbidity and reduces efficiency. *T. H. Davey*

Dastur, D. K. **Microfilarial Lesions in the Human Brain. A Case Report.** *Indian J. Med. Sci.* 1954, Oct., v. 8, No. 10, 709–11.

Involvement of the nervous system in filariasis has seldom been reported. A case is here described in a man of 20 who died in delirium in Bombay. Significant microscopic findings were restricted to the liver and brain. Haemorrhagic necroses were found in the former and fragments of microfilariae in the exudate. In the brain a small cellular nodule was detected in one section of the cortex, consisting of a small collection of neutrophils and microglial histiocytes around two fragments of a microfilaria. A larger area was found in the hippocampal cortex where again portions of microfilariae were found surrounded by a similar exudate.

The question is discussed whether the microfilariae in the brain could have migrated into entirely unrelated areas of focal brain necrosis. If this were the case one would expect to find other lesions without microfilariae in the brain. Despite examination of large numbers of sections only these two lesions were encountered and both showed centrally situated larvae. The pathological reaction in the brain was consistent with an acute focal necrosis caused by a small foreign body. [As microfilariae of *W. bancrofti* are distributed throughout all organs of the body this latter explanation does not appear probable.] *Philip Manson-Bahr*

See also p. 409, Faure *et al.*, Considérations sur l'éosinophilie tropicale [**Observations on Tropical Eosinophilia**].

Hughes, M. H. **Some Observations on the Pathology of Onchocerciasis.** *West African Med. J.* 1954, Dec., v. 3 (n.s.), No. 4, 157–61.

Although onchocerciasis is widely distributed in Africa and Central America there appear to be only 9 records of cases in which search has been made after death for microfilariae in the internal organs. Among these, Rodhain and Gavrilov [this *Bulletin*, 1936, v. 33, 595] found microfilariae, believed to be those of *O. volvulus*, in the breast, spleen, kidney and mesentery as well as in the portal tracts and capillaries of the liver, but Strong later was sceptical of their identity.

Among 414 autopsies performed in Accra from 1949 to 1951 there were 6 cases of onchocerciasis, and microfilariae, believed to be those of *O. volvulus*, were found in the investing membranes of the testes in 2 out of

the 4 in which sections were made. In the third, one testis was abnormal and microfilariae of *O. volvulus* were present in an associated hydrocele. In the fourth, microfilariae were present in the testes, but their identity was uncertain.

This is the first record of the occurrence of these microfilariae in the testis. It is interesting in view of the fact that onchocerciasis is associated with serious depopulation in central districts of the Northern Territories of the Gold Coast, while in the Volta River district, which is infected with *Onchocerca*, the population has also declined since the first census in 1891.

The discovery of microfilariae in the testis suggests the possibility that the direct effects of the parasite on male fertility may be a factor in depopulation. The evidence that microfilariae of *O. volvulus* may be present in the internal organs appears to be very slight. In the sections the basic lesion of onchocerciasis found was cellular infiltration around the small blood vessels of the skin, tunica albuginea, sclera and conjunctiva of the eye. The reason for this perivascular " cuffing " is by no means clear.

Details are given of the 6 cases. *Philip Manson-Bahr*

HUTTON, P. W. **Severe Onchocercal Dermatosis responding to Suramin and Diethylcarbamazine: an Illustrative Case.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1954, Nov., v. 48, No. 6, 522–5, 5 figs. on 2 pls. [11 refs.]

An adult male immigrant from Ruanda Urundi complained of an irritating skin eruption for the previous 3 years. On examination he had generalized thickening of the skin of the back, thighs and knees, the right arm, shoulder and pectoral region, with thickened plaques over the right arm and shoulder and the thighs. There was axillary and inguinal lymphadenopathy and an eosinophilia of 2,700 per cmm. The appearances were those of onchocercal dermatosis, although skin snips and histological sections of skin were negative for microfilariae, as often happens in this type of case.

He was treated at first with diethylcarbamazine, receiving a total of 9 gm. in 20 days. Although his appearance did not change greatly his symptoms cleared after a severe initial reaction, only to recur 11 months later. His relapse was eventually treated with antrypol 9 gm. in 40 days, and diethylcarbamazine 22·2 gm. in 37 days. There was complete remission of symptoms after this treatment and his skin remained normal for a period of 6 months. A high eosinophilia also disappeared. The author considers that the use of the two drugs, suramin to kill the adults, and diethylcarbamazine to clear the remaining microfilariae, appears capable of curing the condition. *H. T. H. Wilson*

See also p. 366, GARFINKEL, *et al.*, **The Role of *Endamoeba histolytica* and *Trichuris trichiura* in Bloody Diarrhea of Children in Puerto Rico.**

DEFICIENCY DISEASES

PALLISTER, R. A. **The Electrocardiogram in Oriental Beriberi.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1954, Nov., v. 48, No. 6, 490–94, 2 figs. [11 refs.]

Patients with beriberi in North America and Europe, especially those who are chronic alcoholics, frequently have electrocardiographic changes.

Abnormalities of the T wave and prolongation of the Q-T interval are common. Aalsmeer [this *Bulletin*, 1951, v. 48, 828] found no significant electrocardiographic changes in 15 patients with beriberi, all of whom were well-to-do-persons in Java, who had lived upon one-sided polished rice diets, but were not alcoholics. This paper describes changes found in 25 Asiatics with beriberi studied in Penang over the last 5 years. These cases have occurred sporadically and the disease has not been common. Abnormal electrocardiographic records were present in 16 of the patients. Inversion of the T wave was the most frequent abnormality and prolongation of the Q-T interval was also common. The changes were essentially similar to those described in cases of cardiac beriberi in the West.

[The author makes no attempt at an explanation of the difference between his findings and those of Aalsmeer. As we are still ignorant of much of the physiological pathology of beriberi, of the underlying chemical changes and of all the dietary factors involved, the point is important. Further electrocardiographic studies in beriberi with full details of the associated cardiovascular signs and of the previous dietary history will be of great interest.] *R. Passmore*

Chhuttani, P. N. **Vegetarians and Malnutrition.** *Indian Med. Gaz.* 1954, May, v. 89, No. 5, 289–92.

In the author's experience when serving with the Indian Army in the Middle East during the 1939–45 war, the numbers of cases of severe anaemia were about the same in vegetarian and meat-eating sepoys. Yet only about 6 per cent. of the sepoys were vegetarians. Clearly the vegetarians were much more susceptible to severe anaemia. Many other observers would agree with this finding. Laboratory studies have indicated that the biological value of the proteins in good mixtures of cereals and pulses are as high as most animal proteins, but the author points out that this is not a completely satisfactory justification for vegetarianism. He adds that there was strong evidence to suggest that a weekly meat ration of 20 oz. of fresh meat made considerable difference to the state of nourishment of a hard-working soldier population. *R. Passmore*

Satoskar, R. S. & Lewis, R. A. **Plasma Protein Pattern of Indian Students. Relation to Diet and Previous Illness.** *Indian J. Med. Sci.* 1954, Oct., v. 8, No. 10, 663–70. [22 refs.]

Plasma protein levels were estimated in 100 Indian medical students, by means of specific gravity and electrophoretic methods. The mean values in gm. per 100 ml. were albumin 4·52, *alpha 1* globulin 0·19, *alpha 2* globulin 0·32, *beta* globulin 0·81 and *gamma* globulin 1·86. These figures all fall within limits usually regarded as normal, except the value for *gamma* globulin which is about double North American and European values. Levels of *gamma* globulin could not be associated with any history of previous disease, but high levels (1·90 gm./100 cc.) were found in vegetarians and lower levels (1·79 gm./100 cc.) in meat eaters and those who took little *dal*. It is concluded that the nature of the dietary protein determines in part the levels of *gamma* globulin.

[The extreme care with which the chemical side of this investigation was carried out contrasts with the apparently casual collection on the dietary data. These figures will certainly serve as a useful standard of normality for Bombay, but it is doubtful whether the dietary information was sufficiently precise to warrant the statistical treatment.] *R. Passmore*

Satoskar, R. S. & Lewis, R. A. **The Effect of Vitamin B12 and Antibiotic Dietary Supplements upon the Plasma Proteins of Indian Medical Students.** *Antibiotics & Chemotherapy.* New York. 1954, Nov., v. 4, No. 11, 1152–8.

This is a continuation of a previous study [above]. Nine of the normal medical students were given oxytetracyline (terramycin) 50 mgm. a day for two months. The serum albumin level rose from 4·18 (standard error, 0·06) to 5·17 (s.e., 0·11) gm./100 ml. The serum *gamma* globulin level fell from 1·92 (s.e., 0·06) to 1·62 (s.e., 0·10) gm./100 ml. A dose of vitamin B12 10 μgm. daily for a similar period had no significant effect of plasma protein levels. The possible relationship between the intestinal flora and protein metabolism is briefly discussed. *R. Passmore*

Baliga, B. R., Rajagopalan, R. & Shivaramaiah, K. **Nutritive Value of Safflower Seed Cake Proteins.** *Indian J. Med. Sci.* 1954, Oct., v. 8, No. 10, 704–8. [17 refs.]

The search for new sources of vegetable protein in India proceeds. This paper records detailed analyses of the cake remaining after expression of the oil from safflower seeds. [The botanical name of the plant is not given.] The biological value of the protein, as determined by the nitrogen balance method of Mitchell on rats, was 86, which is almost as high as that of casein. Chromatographic analysis showed that the protein was a satisfactory source of cystine, methionine and other essential amino acids. The cake also contained valuable amounts of the B group of vitamins and minerals. Clearly it is good food from the chemist's view-point, but the authors make no mention of its taste. *R. Passmore*

André, L. M. & Ganzin, M. Étude préliminaire de la prévention possible des carences protidiques par les lipides végétaux riches en carotène. [**Preliminary Study of the Possible Prevention of Protein Deficiency by Vegetable Lipids rich in Carotene**] *Bull. Soc. Path. Exot.* 1954, v. 47, No. 4, 597–614.

In parts of equatorial Africa near Brazzaville the consumption of palm oil rich in carotene is high. Kwashiorkor is not common in these parts and the authors suggest that this vegetable oil is in part able to offset the effects of protein deficiency. *R. Passmore*

Demaeyer, E. M. & Vanderborght, H. Evolution de la courbe pondérale et de certains constituants biochimiques et hématologiques du sang dans le kwashiorkor. [**Evolution of the Weight Curve and of Certain Biochemical and Haematological Constituents of the Blood in Kwashiorkor**] *Ann. Soc. Belge de Méd. Trop.* 1954, Aug. 31, v. 34, No. 4, 417–32, 4 figs. [30 refs.]

This paper records changes in 79 children with kwashiorkor following upon a dietary treatment previously described [Demaeyer, this *Bulletin*, 1955, v. 52, 79]. All the children were admitted to hospital in Katana, Belgian Congo.

The children were below standard weight on admission. Nevertheless, they lost more weight during the first two weeks of treatment owing to the disappearance of oedema. In 14 children aged 1½–2 years, the mean loss

attributable to the disappearance of oedema was 0·94 kgm., 11·5 per cent. of the initial weight. Thereafter these children gained weight at an average rate of 19 gm. per day; the normal daily gain in weight for children of this age is 6·3 gm. Older children had somewhat less oedema, but gained weight even faster—up to 31 gm. per day.

The changes in the mean levels of plasma proteins were as follows:—

	Total Protein gm. %	Albumin gm. %	Globulin gm. %	*Gamma* globulin gm. %
Before treatment	4·51	1·70	2·81	1·48
After treatment	6·80	3·31	3·49	1·72

Serum amylase rose from 82 to 183 units. Total serum cholesterol rose from 88 to 125 mgm. per 100 ml. of blood. The haematological changes were:—

	Red blood corpuscles per cmm.	Haemoglobin gm. %	Mean corpuscular volume	Mean corpuscular haemoglobin concentration %
On admission ...	3,134,000	8·30	98	27·6
On discharge ...	3,770,000	8·45	90	25·6

Statistical data indicating the range of variations round these mean figures are given. The paper thus provides data which others may find valuable in assessing the response to treatment of individual children.

R. Passmore

Senecal, J., Toury, J., Le Monze, M. & Camain, R. Deux cas de fibrose kystique du pancréas chez l'enfant africain réalisant le syndrome du kwashiorkor. [**Two Cases of Fibrocystic Disease of the Pancreas in African Children, producing the Syndrome of Kwashiorkor**] *Bull. Méd. de l'Afrique Occidentale Française.* 1954, v. 11, No. 1, 95–9, 1 fig.

In both children the clinical features, oedema, enlarged liver, diarrhoea, etc., were characteristic of kwashiorkor. The children did not respond to treatment and rapidly died. Histological examination revealed fibrocystic disease of the pancreas. The differential diagnosis may be very difficult, if not impossible, in life.

R. Passmore

Bras, G., Jelliffe, D. B. & Stuart, K. L. Endophlebitis obliterans hepatica en de daardoor veroorzaakte juveniele levercirrhose. [**Endophlebitis Hepatica Obliterans and Consequent Juvenile Cirrhosis of the Liver**] *Nederl. Tijdschr. v. Geneesk.* 1954, Aug. 21, v. 98 (iii), No. 34, 2341–9, 6 figs. on 2 pls. [40 refs.] English summary.

Histories are given of 12 cases of acute enlargement of the liver occurring in children aged 10 months to 9 years living in Jamaica. The enlargement of the liver was associated with ascites of variable extent, and icterus was also present in some cases. Two patients died from hepatic insufficiency; the others recovered after treatment in hospital for up to 6 weeks. Examination of liver biopsy specimens and material from the fatal cases showed swelling of the intima of the branches of the hepatic vein, fibrosis, and fatty degeneration of the liver epithelial cells. The disease is common in Jamaica and is not related to nutritional status; in a discussion of the aetiology poisoning from the consumption of "bush tea" was considered to be a likely cause. [See also this *Bulletin*, 1954, v. 51, 972, 973.]

D. J. Bauer

Walters, J. H. & Waterlow, J. C. **Fibrosis of the Liver in West African Children.** *Med. Res. Council Spec. Rep. Ser. No. 285.* 71 pp., 6 figs. & 43 pls. [Numerous refs.] 1954. London: H.M. Stationery Office. [8s. 6d.]

This report is compounded of classical morbid histology, clinical medicine and field epidemiology in about equal parts with a touch of modern enzyme biochemistry to taste. The mixture makes fascinating, even exciting, reading. The story runs thus. Fibrosis of the liver is common among children and adolescents all along the Gambia. Fatty degeneration of the liver is, however, not frequently seen, nor is the disease kwashiorkor. However, each year the children have to pass through a hungry season, when food is always scarce and often insufficient. Many of them are obviously undernourished. Malaria is hyperendemic and among the young children infections with *Plasmodium falciparum* are the rule. It is postulated that the combined action of an insufficient diet and a heavy malarial infection is responsible for the fibrosis. Both the nutritional and malarial factors have their most weighty impact on the child in the second year of life. The hypothesis is put forward that malaria causes a localized inflammatory reaction in the portal tracts. If at the same time there is a nutritional injury to the liver, the fibrosis evoked in the first place by malaria may spread into the parenchyma. The liver then develops an active periportal fibrosis. Normally, with an improvement in nutrition, this lesion heals, leaving nothing but residual scars, which may be regarded as evidence of chronic malarial infection. In a few children as a result of continuing or periodic malnutrition, healing does not occur; the fibrosis progresses and becomes diffuse.

The description of the histogenesis of hepatic fibrosis is built up on a study of large amounts of material collected by needle biopsy of the liver. Photomicrographs of 42 sections have been beautifully reproduced and these are used to illustrate the histological arguments step by step. For the most part they are clear. It is unfortunate that biopsy technique provides only such small amounts of material. More low power views of the general architecture of the liver would have been interesting.

The report shows that the chief characteristic of fibrosis of the liver in the Gambia is its complexity. Neither the aetiology nor the histogenesis can be expected to follow along the same lines in each case. The hypothesis of a dual aetiology—nutritional and malarial—appears consistent with the main findings, but does not preclude the possible importance of other as yet unidentified factors. The hypothesis has the merit that it can pave the way to active policies for prevention. *R. Passmore*

VENOMS AND ANTIVENENES

Corkill, N. L. & Kirk, R. **Poisoning by the Sudan Mole Viper *Atractaspis microlepidota* Günther.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1954, Sept., v. 48, No. 5, 376–84, 2 figs. [27 refs.]

An interesting account is given of the natural history of snakes of the genus *Atractaspis*, the mole vipers. Brief clinical histories are given of 12 cases of bites by *A. microlepidota*, 3 of which were fatal. The fatal cases included a man bitten by a very large snake, and two very young sisters. Eleven cases of bite from congeners are also recorded. Tests are

described on the venom from one snake. The venom was dried over calcium chloride and taken up in distilled water. Subcutaneous inoculation into mice indicated that the minimum lethal dose was of a high order. No appreciable spreading factor, proteolytic enzymes, coagulant or haemolytic elements were demonstrated.

The authors conclude that the bite from *Atractaspis* is only occasionally lethal and is not as dangerous as its folk reputation suggests. The area bitten becomes numb; swelling and necrosis of the local skin may follow. The haemorrhagic characteristics of viperine poisoning in general are not evident. Erythrocytes appear early in the urine after the bite, and the authors suggest that microscopic examination of the urine might help the diagnosis and possibly act as a guide to prognosis. *B. G. Maegraith*

Wood, J. T. **A Survey of 200 Cases of Snake-Bite in Virginia.** *Amer. J. Trop. Med. & Hyg.* 1954, Sept., v. 3, No. 5, 936–43. [11 refs.]

This paper is a summary of data from 200 cases of snake bite occurring in Virginia, between 1941 and 1953. The snakes concerned were mostly copperheads. *Ancistrodon contortrix mokeson*, or rattlesnakes. Ninety-six per cent. of bites recorded occurred in the period May to September, with a peak in July. Most bites thus occurred in the months when snakes are active at night and in concealment by day. Nevertheless, two bites occurred by daylight for every one at night. Those during the day were most frequent on the upper extremities, those at night on the lower. About half were received by persons under 16 years of age. All except 4 of the cases recorded were in persons admitted to hospital. In those who were not, 3 deaths were recorded [these included 2 cases other than the 200 of the series]. No fatalities were recorded in the hospitalized series. Of the 168 cases in which therapeutic data were available, 90 per cent. received antivenene. Those patients who did not receive it were either strongly sensitive to horse serum or treated where antivenene was not available.

B. G. Maegraith

TOXOPLASMOSIS

Jírovec, O. & Jíra, J. Versuch einer einheitlichen Auffassung der Epidemiologie und Pathogenese der Toxoplasmose. [**Studies on a Unified Conception of the Epidemiology and Pathology of Toxoplasmosis**] *Zent. f. Bakt.* I. Abt. Orig. 1954, v. 161, Nos. 7/8, 521–31, 1 fig.

This paper from Prague postulates that the clinical conditions caused by toxoplasms in the human being depend upon the number of organisms in the infecting dose, a few organisms producing chronic or latent infection and a large number causing acute toxoplasmosis. With this assumption the authors show diagrammatically how the various known manifestations of toxoplasmosis, ranging in severity from a trace of antibody in the serum to a fulminating and fatal neonatal illness, are associated and may be the logical development of one another. Continuing parasitaemia, the rupture of pseudocysts, reactivation of latent infections by conditions such as pregnancy, and the part played by the toxoplasm exotoxin, all contribute to this unified conception of toxoplasmosis.

Some consideration is given to the natural toxoplasm reservoirs in nature

and the mode of infection of man, and figures are cited which show that the incidence of toxoplasmosis in Czechoslovakia is similar to that reported from almost all other countries; the authors emphasize the clinical importance of differentiating between serological evidence of infection with toxoplasms and illness caused by them. *I. A. B. Cathie*

Holz, J. Die Vermehrung von *Toxoplasma gondii*. [**Multiplication of** *Toxoplasma gondii*] *Ztschr. f. Hyg. u. Infektionskr.* 1954, v. 140, No. 2, 134–7, 5 figs.

Previous studies of *Toxoplasma gondii* in bone-marrow cultures, in stained preparations, and by electron microscopy, have shown that this parasite multiplies by longitudinal binary fission. The investigation described in the present paper was carried out in order to elucidate cytological details of this process. For this purpose, mice infected with toxoplasms were treated with colchicine, which has the effect of inhibiting mitotic nuclear division, thereby enabling the chromosomes to be counted. In the peritoneal exudate of mice thus treated the nuclei of the parasites were found to be in the metaphase stage, containing 6 chromosomes, as in Myxosporidia and some Coccidia. It was also confirmed that the toxoplasms multiply intracellularly by repeated binary fissions, in the course of which the nucleus divides mitotically, and there was no evidence of multiple division.

Finally, the author discusses the affinities of *Toxoplasma*, and points out that the longitudinal plane of division separates it from the ciliates, while binary fission differentiates it from most Sporozoa, though the method of locomotion in some stages of the latter group (*e.g.*, coccidial sporozoites and plasmodial oökinetes) is comparable to that in *Toxoplasma*. The division and chromosome constitution of this parasite are depicted in a number of figures. *C. A. Hoare*

Vischer, W. A. & Suter, E. **Intracellular Multiplication of** *Toxoplasma gondii* **in Adult Mammalian Macrophages cultivated** *in vitro*. *Proc. Soc. Exper. Biol. & Med.* 1954, July, v. 86, No. 3, 413–19, 7 figs. [10 refs.]

The authors describe observations on the development of *Toxoplasma* in macrophage cultures. Macrophages of laboratory rodents were obtained from the peritoneal exudate a week after intraperitoneal injection of a chemotactic agent (glycogen or sodium caseinate). Cultures were prepared as follows: (a) the cell suspension in Gey's balanced salt solution, containing heparin, was poured into Petri dishes, at the bottom of which were placed coverslips; (b) the toxoplasms from the peritoneal exudate of an infected mouse, mixed with the same salt solution, were freed of the host-cells by squeezing through a narrow-gauge syringe, followed by centrifugation; and (c) they were inoculated in the dishes in the proportion of one parasite per 7 macrophages. The dishes were incubated for 1–2 hours at 37°C., after which each coverslip was removed, washed in the salt solution, covered with a film of "formvar", and placed in a screw-capped vial containing culture medium and rodent serum, together with amounts of streptomycin and penicillin which inhibited contamination but had no harmful effect on the toxoplasms. The coverslip cultures were removed for examination at regular intervals and fixed in absolute methyl alcohol, after which the "formvar" was removed from the back of the slide, and the preparations were stained with haematoxylin and mounted. Rats and

guineapigs were immunized by repeated subcutaneous inoculations of living toxoplasms, and the presence of antibodies in the serum was determined by the dye test.

The observations made on the infected macrophage cultures were as follows. First the parasites found their way into the macrophages, where they multiplied, finally rupturing the host-cells and becoming free, after which they infected new macrophages and the cycle was repeated. It was shown that the macrophages phagocytose the parasites, but these actively penetrate into other parenchymal cells. The phagocytic activity of macrophages from various rodents was different, and could be correlated with the susceptibility of the host to infection with *Toxoplasma*. It was also found that macrophages from animals immunized against toxoplasms inhibited the intracellular multiplication of the parasites *in vitro*. Since this effect was greater when immune serum was combined with immune cells than when it was combined with normal macrophages, it is concluded that both cellular and humoral factors are involved in the mechanism of immunity. The appearance of *Toxoplasma* in the cultures is depicted in a series of photomicrographs. *C. A. Hoare*

Kunert, H. & Schmidtke, L. Inhalationsversuche mit *Toxoplasma gondii*. [**Transmission of *Toxoplasma* by Inhalation**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1954, July, v. 5, No. 3, 324–9, 2 figs. [12 refs.]

Up to the present the natural method of transmission of toxoplasmosis, except that acquired *in utero*, has remained unsolved. Experimental attempts to produce infection by mouth and through blood-sucking arthropods have given doubtful results. However, the detection in some animals of parasites in the faeces and urine, on the one hand, and in oral and nasal secretions, on the other, suggested the possibility of contaminative and droplet transmission, respectively. Furthermore, in man, as well as in some animals, the finding of toxoplasms in macrophages of the pulmonary alveoli and bronchioles [this *Bulletin*, 1941, v. 38, 533] seemed to support the supposition that toxoplasmosis might be transmitted through the saliva.

The experiments described in the present paper were designed to throw light on transmission of toxoplasmosis by the droplet method. After trying out various methods, the authors arrived at the following experimental techniques: in the case of mice, each animal was placed within a glass cylinder covered with wire gauze at the open end, while guineapigs were placed in cylindrical tubes, 4 of which were screwed into a special inhaling chamber. To prevent their displacement, the space around the animals was packed with " cellulose ", while their eyes were protected from infection by adhesive tape. In these experiments the animals were exposed to inhalation—for 10 minutes to 1 hour—of finely vaporized peritoneal exudate of infected mice, which was sprayed from a pocket glass sprayer. The results were assessed, in doubtful cases, by subinoculation of mice with organ suspensions of the experimental animals and by the dye test. Infection was produced by this method in 8 out of 9 guineapigs, 6 of which died, while 2 had a latent infection revealed by the dye test. However, the results with mice were inconclusive, owing to the unsuitability of the technique used, but the susceptibility of these animals to infection by the nasal route has already been demonstrated [this *Bulletin*, 1955, v. 52, 199].

It is concluded that droplet transmission of human toxoplasmosis might conceivably also take place, in patients with pneumonitis, though it would hardly account for the wide incidence of latent infection in man.

C. A. Hoare

Havlík, O. & Zástěra, M. Toxoplasmosa jako ohnisková nákaza. [**Toxoplasmosis as a Focal Infection**] *Československ. Hyg., Epidemiol., Mikrobiol., Imunol.* Prague. 1954, v. 3, No. 4, 214–18, 4 figs. on 2 pls. [15 refs.] English summary.

Marmots were found to be susceptible to toxoplasmosis and died 5 to 10 days after intraperitoneal inoculation of the parasite. Two of 4 animals infected orally died after 7 and 8 days with specific pneumonia, possibly as a result of inhalation of part of the inoculum. Four marmots infected at the beginning of hibernation died of generalized toxoplasmosis after awakening, after intervals of 20, 41, 84 and 88 days, respectively, and the infection could presumably be maintained in natural conditions in this way.

Two young foxes which ate heavily infected mice and 1 inoculated with the parasites intraperitoneally showed no signs of infection. *Toxoplasma* infection was demonstrated serologically in 3 of 7 hedgehogs (*Erinaceus europeus*, *E. roumanicus*) caught in the neighbourhood of Prague and Beroun. *D. J. Bauer*

Giroud, P., Giroud, A. & Martinet, M. Répercussions de l'inoculation de toxoplasme à des rattes gestantes. [**Effects of Inoculation of Pregnant Rats with Toxoplasms**] *C.R. Soc. Biol.* 1954, June, v. 148, Nos. 11/12, 1030–31.

Female rats were inoculated with a human strain of *Toxoplasma gondii* between the 1st and 11th days of pregnancy. The infection was symptomless, and they were sacrificed on the 21st day with the view of studying the effect of the infection on the foetuses. Abortions occurred in 25 to 55 per cent. of cases, while up to 68 per cent. of the surviving foetuses showed lesions of the lens, including cataracts. *C. A. Hoare*

Desmonts, G. & Le Tan Vinh. Sur la réaction de fixation du complément au cours de la toxoplasmose du cobaye. [**Complement-Fixation Reaction in Toxoplasmosis of Guineapigs**] *C.R. Soc. Biol.* 1954, June, v. 148, Nos. 11/12, 1000–1002.

An account is given of an investigation on the specificity of the complement-fixation test in experimental toxoplasmosis of guineapigs. All the animals had been tested serologically before inoculation, when it was found that about 10 per cent. of 168 laboratory-bred guineapigs and 2 of 12 obtained from dealers reacted positively.

The complement-fixation reaction in guineapigs becomes positive when the animals survive the acute phase of the experimental infection, manifesting itself between the 12th and 20th days after inoculation and persisting for more than a year after recovery. As regards the apparently healthy guineapigs with a positive reaction, they proved to have a cryptic infection, which was revealed by the finding of pseudocysts in their brain and by subinoculation into mice. It is concluded that the complement-fixation reaction is a reliable test for toxoplasmic infection in guineapigs. Hence the positive results obtained in apparently normal animals point to the occurrence of natural infections in these animals, which should be taken into consideration when interpreting the results of inoculation of guineapigs for diagnostic purposes. *C. A. Hoare*

Jacobs, L. & Cook, M. Katherine. **Variations in the Dye Test for Toxoplasmosis.** *Amer. J. Trop. Med. & Hyg.* 1954, Sept., v. 3, No. 5, 860–67.

Though the Feldman and Sabin dye test for toxoplasmosis is generally reliable and provides consistent results, in some cases there is considerable variation in the titres obtained and the proportion of stained and unstained parasites. Using a standardized procedure, the authors have endeavoured to analyse and elucidate the factors responsible for the interference or inhibition of the dye-test reaction, and have presented the results of this investigation in 7 tables. It would appear that neither the brand of methylene blue employed nor the number of parasites present in the peritoneal exudate has any influence upon the reaction. However, it was found that, after removal of the toxoplasms and cellular elements from the peritoneal exudate by sedimentation, the supernatant fluid, when added to the dye-test reaction mixture, caused complete inhibition of the reaction. It is concluded that this phenomenon was due to the presence, in the peritoneal exudate of mice, of a component representing soluble antigen. Though, as a rule, the amount of this protein is not sufficient to obscure the dye test, its concentration is subject to variation, thereby affecting the course of the reaction in some cases. *C. A. Hoare*

Müller, F. Experimentelle Untersuchungen über das Verhalten der Toxoplasmoseantikörper bei einer anderen Infektionskrankheit. [**Experimental Study of the Behaviour of Toxoplasma Antibodies in the Presence of another Infective Condition**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1954, Nov., v. 111, No. 5, 401–8, 1 fig.

Working in the Hygiene Department of Leipzig University, the author undertook experiments to test the theory that when a latent toxoplasma infection is present an infection with another organism will cause an anamnestic rise in the toxoplasma antibody as shown by a rise in the Sabin and Feldman dye test for toxoplasmosis. Rats were infected intraperitoneally with toxoplasmas and the subsequent dye-test titres reached a peak in 10–14 days. Thereafter the rats were given 5 injections of a killed suspension of typhoid bacilli at 2-day intervals. For 5 weeks after the typhoid injections were started Widal reactions as well as toxoplasma dye tests were carried out twice weekly. Tables and graphs show that the steady increase in titre of typhoid antibodies did not interfere with the steady decrease in the dye-test titre; apart from a very slight and transient rise in the dye-test titre about a fortnight after the typhoid inoculations were started the anticipated anamnestic rise in the dye-test titre was not seen. *I. A. B. Cathie*

Paulley, J. W., Jones, R., Green, W. P. D. & Kane, E. P. **Myocardial Toxoplasmosis.** *Lancet.* 1954, Sept. 25, 624–6. [18 refs.]

The authors refer to previously published work on toxoplasmosis affecting the myocardium and point out that myocarditis without an obvious cause is not very uncommon. As an example they refer to the endomyocardial fibrosis which has been the object of much study in Africa recently [Bedford and Konstam, *Brit. Heart J.*, 1946, v. 8, 236; Higginson, *et al.*, *ibid.*, 1952, v. 14, 213; Gillanders, this *Bulletin*, 1953, v. 50, 141; Ball *et al.*, *ibid.*, 1954, v. 51, 839], and suggest that in view of their observations on toxoplasmosis this infection should be considered in such cases.

Three cases are then described. In the first the patient was mentally dull, he had auricular fibrillation and gross left bundle-branch block, a large pleural effusion, a large pulmonary conus and very large right and left ventricles. He later developed hemiplegia. The dye test for toxoplasmosis was positive at a dilution of 1 in 64 and the complement-fixation test at 1 in 16. There was no cerebral calcification. Several members of this patient's family had died suddenly or suffered from some degree of mental deficiency. Post-mortem examination of one sister had revealed " . . . myocarditis of unusual type. . . . Severe cloudy swelling of hypertrophied fibres, slight fatty change, areas of dense young fibrous tissue, and diffuse fibrosis with focal non-specific chronic inflammation in myocardium of both ventricles, and with endocardial thrombosis. . . . The condition appears to be a non-specific myocarditis in the healing phase following severe focal necrosis ". The second patient had an irregular pulse, engorged neck veins, enlargement of the heart and his serum gave a positive dye test at a dilution of 1 in 32 and a positive complement-fixation test at 1 in 16. The third patient was symptom-free, and had good exercise tolerance, but cardiomegaly was present and the dye test was positive at a dilution of 1 in 512 and the complement-fixation test at 1 in 32. The patients were all males aged 24 to 39 years.

Although definitive proof of toxoplasmosis was lacking, the history, the dye and complement-fixation tests, and in the first case the family history, all strongly suggested the diagnosis. The difficulty of finding toxoplasmas in infected tissue is discussed and a case is quoted in which only 3 pseudocysts were found in 220 sections of heart muscle.

This is an important paper in view of the light which it may throw on endomyocardial fibrosis in Africa. *A. W. Woodruff*

Cathie, I. A. B. **Myocardial Toxoplasmosis.** [Correspondence.] *Lancet.* 1955, Jan. 15, 149.

The author refers to the cases reported by Paulley *et al.* [above, p. 400] which were diagnosed as toxoplasma myocarditis as a result of positive dye and complement-fixation tests. After that report had been published, the present author received in his laboratory a number of sera from patients with obscure myocarditis, for examination for toxoplasma antibodies. In one case the dye and complement-fixation tests were positive at 1 in 32 and 1 in 8 respectively and these were regarded as diagnostic titres. The patient died soon afterwards and it was possible to inject mice intraperitoneally with washed and ground myocardial tissue: 10 days afterwards abundant toxoplasms were seen in the mouse peritoneal exudate and could be passaged therefrom.

The association between the toxoplasma antibodies in the serum and the toxoplasms in the tissues is thus emphasized and the diagnosis of toxoplasmosa myocarditis in the cases of Paulley *et al.* made on serological grounds, is supported. *H. J. O'D. Burke-Gaffney*

Eyles, D. E. & Coleman, Nell. **Notes on the Treatment of Acute Experimental Toxoplasmosis of the Mouse with Chlortetracycline and Tetracycline.** *Antibiotics & Chemotherapy.* New York. 1954, Sept., v. 4, No. 9, 988–91.

Mice were inoculated with 20,000 *Toxoplasma* organisms (about 1000 lethal doses) and treated forthwith and for 14 days by aureomycin [chlortetracycline] added to their food. On an extremely large dose, 800 mgm. per

cent. in the diet, equivalent to 1600 mgm. per kgm. per day, 66·7 per cent. of mice were cured, not only surviving for 42 days, but being free of infection as indicated by inoculation of other mice with brain and liver suspensions. A dose of 400 mgm. per cent. in the diet cured 13·9 per cent., 200 mgm. per cent. cured only 2·8 per cent., and 100 mgm. per cent. cured none. A similar experiment was done with tetracycline: 800 mgm. per cent. cured 8·3 per cent. and lower doses none, although the next lower dose prolonged survival. Tetracycline is thus much less effective than chlortetracycline in this infection. Owing to the dangerously large doses required, these findings have no clinical application, but the authors think they should encourage the testing of other broad spectrum antibiotics for this purpose. [For previous experimental therapeutic studies by the authors, see this *Bulletin*, 1953, v. 50, 568, 569, 980; 1954, v. 51, 1190, *bis.*]

L. P. Garrod

DERMATOLOGY AND FUNGUS DISEASES

Creitz, J. R. & Puckett, T. F. **A Method for Cultural Identification of *Coccidioides immitis*.** *Amer. J. Clin. Path.* 1954, Nov., v. 24, No. 11, 1318–23, 5 figs. [13 refs.]

The risk of air-borne infection from sporing cultures of *Coccidioides immitis* is shown by the records of 16 cases of laboratory infection reported in the literature [see Smith and Harrell, this *Bulletin*, 1948, v. 45, 814; Looney and Stein, *ibid.*, 1950, v. 47, 492] and an additional 63 proved and 9 probable cases communicated to the authors by C. E. Smith. Because of this hazard, culture methods for the diagnosis of coccidioidomycosis are forbidden in some laboratories. The present authors have devised a system in which diagnosis by isolation of *C. immitis* can be made with the minimum risk of infection.

C. immitis develops rapidly in culture at 37°C. on many different agar media; measurements of growth on various media made at daily intervals are set out in a table. Spores are present in cultures about 6 days old and handling such cultures may entail some risk of infection, but young cultures, 3 or 4 days old, can be picked off with safety and subcultured. In the primary growth from a sowing of morbid material containing *C. immitis* it may be difficult to distinguish the young colonies of this species from those of contaminant fungi, but on blood agar it is possible to make a presumptive identification of *C. immitis* colonies when only 48 to 72 hours old. On this medium, in 24 hours at 37°C. the colonies of *C. immitis* are 1 mm. or less in diameter, flat and dark with irregular, fuzzy edges; at 48 hours they measure 1–4 mm. in diameter, are raised and glabrous, the edges are more regular and less fuzzy and the medium immediately under the colony is darkened and may appear purple by transmitted light; at 72 hours the colony is 2–9 mm. in diameter and its surface bears a fluffy aerial growth in wisps and tufts of the future fertile mycelium. Colonies at this stage, from a sowing of morbid material, can be roughly identified, picked off and subcultured into tubes of broth, 2 or 3 colonies to each tube to ensure an abundant growth. If bacterial contaminants are present, antibiotics may be added to the broth medium. After about 7 days' incubation the mycelial growth in the broth medium, which should not contain spores, can be collected, ground up in a mortar and injected intraperitoneally into

mice. The mice are killed in about 6 days and examined for the characteristic spherules and sporangia of *C. immitis*. The identification of the isolate is therefore made on its parasitic phase and not on its saprophytic, sporing form.

The method described was successfully used in the authors' laboratories for the diagnosis of 38 cases of coccidioidomycosis, the morbid materials used being sputum, pus, empyema fluid, exudate from resected cavities, fragments of resected granulomata, bronchial washings and tissues from necropsies.

The identification of *C. immitis* by microscopy in preparations of chronic focalized lesions of man is sometimes difficult, and although cultures may be obtained from the lesions they are not always morphologically typical [see Friedman *et al.*, 1954, v. 51, 222; and Hampson, *ibid.*, 1954, v. 51, 1192]. In such cases the authors' method would have an additional value.

J. T. Duncan

TROPICAL OPHTHALMOLOGY

Blumenthal, C. J. **Blindness and Malnutrition in the Eastern Cape Province.** *South African Med. J.* 1954, Nov. 13, v. 28, No. 46, 967–71, 2 figs.

According to the author's experience malnutritional keratitis is common in the young Bantu [this *Bulletin*, 1950, v. 47, 1127] and a common cause of blindness in the Eastern Cape Province of South Africa. It occurs mainly in the 2–3 years following weaning and the damage is initially stromal, or mesodermal, in origin. He considers that the initial intracorneal softening is caused by a vitamin-B deficiency and the secondary surface catarrh and ulceration by lack of anti-infective vitamin A. It is different from keratomalacia so frequently seen in the Far East, which is also mesodermal in origin; it is independent of any superficial infection in that the conjunctiva does not become smoky, dry or wrinkled. There is in fact an increase of secretion. Marasmus is not typical in malnutritional keratitis, the fat, podgy baby being more in evidence.

A recent assertion that, in the vast majority, corneal scars in the Bantu are the direct result of primary bacterial infection and neglected corneal ulcers, is vigorously contested.

Conjunctivitis caused by the common pathogens—Koch-Weeks bacillus, staphylococcus, pneumococcus, etc.—very rarely leads to corneal involvement in the Bantu. Trachoma is also relatively uncommon, is frequently misdiagnosed and none of its features is specific. Inclusion bodies, on the evidence available, are not diagnostic. Incorrect diet at an early age and not dirt, the author considers, is the important factor in the aetiology of trachoma, but his method of treatment in the true stubborn cases by the application of the copperstick, combined with expression, will not meet with favour by many ophthalmologists. *E. W. O'G. Kirwan*

Falcone, C. **A Tropical Dystrophy.** *East African Med. J.* 1954, Oct., v. 31, No. 10, 471–5, 3 figs.

The author describes a degenerative change in the cornea which he has frequently seen in Somalia and which is very similar to band-shaped opacity. He has named the condition tropical corneal dystrophy.

Out of 16,500 eye patients, the condition was diagnosed in 340 (2 per cent.). About 95 per cent. of the patients were males and the ages varied from 12 years to extreme old age, the commonest age of onset being 30–50 years.

The disease follows a long slow course. The lesions nearly always appear first on the temporal side as a cluster of epithelial bullae. The opacity slowly grows horizontally across the area of cornea exposed by the palpebral fissure; the vesicles become more and more numerous, overlying each other until in the most typical form they come to resemble a cauliflower. The growth assumes a greyish-yellow colour and as it advances fuses with a similar lesion which has developed later on the nasal side of the cornea. The whole of the exposed cornea becomes involved except a narrow portion between the opacity and the limbus as is seen in typical band-shaped keratitis. There is no tendency to superficial or deep vascularization, a fact which rules out the presence of any inflammatory origin to explain the condition. The disease is painless and commonly passes unnoticed by the patient until the prepupillary area is invaded, causing impairment of vision.

The author has not been able to come to a final conclusion as to aetiology. Internal and external factors play their part. Of the former, previous or existing infectious disease or alimentary deficiency in the form of avitaminosis or various forms of slow intoxication, may lead to the essential trophic changes. Among the external factors, the most deserving of study is sunlight, for the solar radiations, rich as they are in ultra-violet rays, are almost totally absorbed by the cornea and are harmful to that tissue. Once the condition is established no therapy is of any avail, except to adopt measures that will reduce the risk of those complications which may lead to blindness. Emphasis must be on prevention and on treating the patient as a whole, the corneal dystrophy being but one sign of a deficiency or dysfunction. *E. W. O'G. Kirwan*

HEAT STROKE AND ALLIED CONDITIONS

Horne, G. O. **The Effects of Environmental Heat.** *Edinburgh Med. J.* 1954, Nov., v. 61, No. 11, 349–66, 4 figs.

The physical aspects of body heat regulation and the physiological adaptations to hot environments are discussed briefly. Limits of tolerance depend on environmental conditions and on the limit of adaptability of the sweating and circulatory systems. The risk of heat casualties is increased among older people, the unfit and the psychologically unadaptable, and among those who lack acclimatization, are dehydrated, consume alcohol or are unsuitably clothed.

A terminology and classification of heat-stress symptoms according to the clinical features are given: (1) heat hyperpyrexia and heat stroke; (2) exhaustion and collapse precipitated by: (a) exercise without dehydration or anhidrosis, (b) dehydration (hypochloraemic), (c) anhidrosis; (3) syncope; (4) muscle cramps; (5) tropical neurasthenia. The syndromes are further classified according to the aetiology, *e.g.*, circulatory deficiency will cause exercise-precipitated heat exhaustion and collapse or heat syncope. Chloride deficiency will cause dehydration (hypochloraemic) heat exhaustion and collapse or muscle cramps. Other syndromes considered are heat oedema, sunburn, pricky heat and simple water deficiency.

Incidence of all types of heat syndromes are given for the years 1945 to 1947 in the hot humid climate of Karachi, India, and for 1943 in the hot dry climate of Shaiba, Iraq. " Even minor variations in the environment may lead to important differences in the total and relative incidence of these syndromes." *Barbara Tredre*

Ellis, F. P. **Some Medical Aspects of Human Climatology in the Equatorial Tropics.** *Brit. Med. J.* 1954, Sept. 4, 549–54. [30 refs.]

The author considers 3 medical aspects of hot climates—skin disease, fatigue and heat incapacitation—and discusses the general principles which underlie their prevention. He draws mainly from the work of the Medical Research Council's team in Singapore.

Prickly heat, pyogenic and mycotic dermatoses are the skin diseases most likely to occur in hot environments. Strict personal cleanliness and frequent and early treatment will do much to prevent and control them. Prevention, however, is difficult in conditions causing continuous sweating. The introduction of air conditioning in submarines and frigates in the tropics resulted in a dramatic reduction in skin disease and other heat illnesses.

Tropical neurasthenia and hot climate fatigue " differ only in degree and chronicity with the proportions of the climatic or neurotic components and the different circumstances under which they are encountered ". Factors such as inertia, monotony, domestic worries and isolation, all add to the climatic effects. Deterioration in mental performance occurred in acclimatized naval ratings in Singapore experiments at temperatures between 78 and 85°F. Observations of men step-climbing revealed the onset and progress of simple acute fatigue with headaches, bad co-ordination and some mental " cloudiness " even in environments below the tolerable limits.

The true incidence of heat incapacitation is probably masked by the transient nature of the condition. Salt-deficiency dehydration states are the most prevalent. The features of heat incapacitation are: (1) water and salt deficiency with cramps, fatigue, circulatory failure and syncope; (2) thermoregulatory failure with rapidly rising body temperature due to: (a) excessive heat, hard work or unsuitable clothing, or (b) anhidrosis, or (c) toxic infections; (3) circulatory failure with a rapid pulse rate and falling blood pressure; (4) acute fatigue, where men are unable to work efficiently despite the relative absence of (1), (2) and (3).

Preventive measures are adequate intake of water and salt to replace that lost in sweat and strict control of the thermal environment. Human variability in salt requirements is stressed. Both a high and a low intake lead to unpleasant symptoms. In the Singapore experiments a salt intake of 1 gm. per litre of sweat lost together with a liberal intake with meals prevented dehydration and increased tolerance. The author recommends that in closed spaces the effective temperature (or corrected effective temperature) should be kept below 78°F. and should not exceed 86°F. A rise of wet bulb temperature of only 2°F. or a decrease in air movement from 150 to 20 ft./min. will change a tolerable into an intolerable environment. A man sitting at rest for 3 to 4 hours will tolerate a wet bulb of 4° to 5°F. higher than if he engages in constant light work. Additional work, clothing, heat-producing machinery or occupants in a room all increase the heat stress imposed on the individual. *Barbara Tredre*

MISCELLANEOUS DISEASES

Beamer, P. R., Varney, P. L., Brown, W. G. & McDowell, F. **Studies on *Malleomyces pseudomallei* isolated from Melioidosis originating in the Western Hemisphere.** *Amer. J. Clin. Path.* 1954, Nov., v. 24, No. 11, 1231–40, 5 figs. [13 refs.]

The authors give a brief general account of melioidosis and describe the clinical findings in two cases believed to be the only ones so far reported as originating in the Western Hemisphere. The first of these has already been noted [McDowell and Varney, this *Bulletin*, 1947, v. 44, 851]. The second patient (Beamer *et al.*, *Amer. J. Path.*, 1948, v. 24, 717 (abstract)) was a white woman, aged 25, who had never been outside the United States. Her infection took the form of spreading necrosis of the skin and deeper tissues of the lower abdominal wall, with involvement of the regional glands. She was treated with penicillin, streptomycin and sulphadiazine but died after a long illness. Autopsy revealed extensive multiloculated abscesses underlying the skin lesion, and small granulomata in the liver and kidneys. *Pfeifferella whitmori* was isolated from the walls of the abscesses. The sera from both patients contained specific agglutinins to a titre of about 1 in 1280.

The characters of the strains from these 2 cases are described in detail. They conform to the usual descriptions. The strains, injected as undiluted broth cultures, were lethal to guineapigs and mice, but, surprisingly, guineapigs survived the injection of 0·5 ml. of culture diluted 1 in 10. Growth of both strains occurred in concentrations of penicillin (250 μgm./ml.), streptomycin (250 μgm./ml.), aureomycin (50 μgm./ml.), chloramphenicol (100 μgm./ml.), streptothricin (one strain) (80 units/ml.). Both strains were slightly inhibited by tyrothricin but it was not bactericidal in concentrations up to the limit of solubility.

[A third case, reported from Wisconsin, has also been noted previously in this *Bulletin* (Garry and Koch, 1952, v. 49, 448).]

J. C. Cruickshank

Ziskind, J., Pizzolato, P. & Buff, E. E. **Characteristics of a Strain of *Malleomyces pseudomallei* from Chronic Melioidosis.** *Amer. J. Clin. Path.* 1954, Nov., v. 24, No. 11, 1241–5, 5 figs.

Pfeifferella whitmori was isolated from an American serviceman, aged 40 years, who had suffered from melioidosis for 5 years following service in the Philippine Islands, Guam and Okinawa. The lungs, liver and bones were affected and the organism was isolated from sputum, the liver, a resected necrotic rib and a gland. Agglutinins were present to a titre of 1 in 16.

The organism, described in detail, conforms to the usual description. It was highly virulent for guineapigs, lethal infections being induced by scratching with a needle dipped in culture. According to tube-dilution tests, the organism was sensitive to tetracycline (1·56 μgm./ml.), oxytetracycline (3·12 μgm./ml.), aureomycin (3·12 μgm./ml.), chloramphenicol (6·25 μgm./ml.), penicillin (25·0 μgm./ml.) and neomycin (50·0 μgm./ml.). Treatment with massive doses of the first 4 of these antibiotics, however, did not halt the disease. The strain was not sensitive to bacitracin, streptomycin, polymyxin, Ilotycin [erythromycin] and Magnamycin [carbomycin] in a concentration of 100 μgm./ml.

J. C. Cruickshank

Mansoor, S. **Two Cases of Favism in Israel.** [Memoranda.] *Brit. Med. J.* 1955, Jan. 15, 149–50.

i. Konstam, P. G. **Peptic Ulceration in Southern Nigeria.** *Lancet.* 1954, Nov. 20, 1039–40. [10 refs.]

ii. Buxton, K. L. **Peptic Ulceration in Tropical Africa.** [Correspondence.] *Ibid.*, Dec. 11, 1231.

iii. Rose, J. R. **Peptic Ulceration in Southern Nigeria.** [Correspondence.] *Lancet.* 1955, Jan. 8, 107.

i. The author reviews 20 consecutive cases of proved peptic ulcer treated in 9 months at Ibadan, a town of 500,000 people situated among hills in the forest zone of the Western Region of Nigeria. The mean rainfall is 48·3 in. annually and the mean maximum and minimum temperatures are 88·5°F. and 70·5°F.

Peptic ulcer has been reported from both the Western and Eastern regions of Southern Nigeria. The author's series comprised 15 males and 5 females, all Africans of the poorer class, their ages ranging from 13 to 65 years. The signs and symptoms were typical of long-standing duodenal ulcer at various stages of cicatrization. Alcohol test meals given to all the patients and to an equal number of controls showed a significant tendency to higher free acid readings in the patients. Liver function tests showed no deviation from the normal and plasma-protein levels were also normal. No gastric ulcer was found in the series, but the exact situation of the duodenal ulcers was difficult to determine on account of extensive fibrous tissue reaction covering the entire first part of the duodenum; however, the ulcers were predominantly posterior-wall lesions, for which reason anterior-wall perforations were rare.

In patients with a high degree of stenosis gastrojejunostomy gave dramatic results. but in the less urgent cases it was difficult to tell from clinical signs, and even from operative findings, whether the ulcer was active or not, so, as stomal ulcer may follow gastrojejunostomy in cases where the ulcer is active, the author treated 13 patients by partial gastrectomy and the remainder by gastrojejunostomy, except for one in which a late anterior perforation was closed. There were 3 deaths.

Discussing the pathogenesis of Nigerian duodenal ulcer the author discounts smoking, hot spices and mental strain as causes; he believes that the ulcers occurring in Nigeria and those in southern India are closely related and caused by geographical and dietary factors. Peptic ulcer is common in the southern regions of rain and deciduous forest, but not in the northern semi-arid plains. The staple diet of the south is cassava and yam, but that of the north is two forms of millet; both diets are deficient in proteins, that of the south particularly so. The yam and cassava diet is deficient in thiamine, contains too much carbohydrate and is very bulky; the almost invariable presence of hookworms and roundworms, which are said to absorb large quantities of B-complex vitamins, leads to further deficiency of this vitamin; there is a deficiency of riboflavin in all parts of Nigeria, but nicotinic acid, ascorbic acid and carotene are in adequate supply.

In India peptic ulcer (predominantly duodenal) is said to be 58 times more common in the south, where the climate is warm and humid and the staple diet consists of rice and tapioca, than in north India where the humidity is low for most of the year and the people live on whole-meal flour, milk and milk products. The author does not consider Nigerian peptic

ulcer to be due to a gross deficiency in thiamine, but to an imbalance of the diet with an intake of vitamin B varying from minimal to sub-minimal.

ii. Following the publication of the paper summarized above, the writer of this letter confirms from his experience in the Ruanda-Urundi territory, Belgian Congo, that peptic ulcer is extremely common among Africans. The area is 6,000–8,000 ft. above sea level and the average temperature about 70°–80°F., with an agricultural and trading population. Peptic ulcer is much commoner in men than in women, and in the poorer classes, a fact which the writer relates to the long interval between meals and to the fact that the men are heavy smokers and drinkers. The diet is deficient in animal protein and there is a high incidence of kwashiorkor in children at 6 months to 2 years, and of cirrhosis in adults; *Ascaris* infection is common. The author disagrees with KONSTAM on the influence of mental strain, which he rates high among factors causing digestive disturbance and ulceration; the people of this district are animists by faith and live constantly in a state of fear—fear of evil spirits and fear of poisoning by their enemies.

Many of the cases seen have advanced to fibrosis and stenosis before coming for treatment, so that gastrojejunostomy produces dramatic and satisfactory results.

iii. Referring to the article by KONSTAM on this subject the author relates his experience of 16 cases of acquired pyloric stenosis in Africans from the south-east province of Sierra Leone, operated upon by him. All gave a long history of epigastric pain with symptoms of advancing pyloric stenosis and in the majority the stomach was found to be huge. All were treated by gastrojejunostomy, except one in whom partial gastrectomy was performed, and in all cases the clinical results of operation were most satisfactory. The operative findings, however, differed from those described by Konstam, in that in place of chronic duodenal ulceration with extensive adhesions around, the author found a prepyloric mass of granulomatous tissue, often ulcerated in the centre. Smears from the surface of this mass showed ova of *Schistosoma haematobium* in nearly half the cases, and the appearance resembled the interior of the urinary bladder in advanced schistosomiasis of that organ; adhesions were very dense and extensive, involving the pylorus, duodenum and neighbouring organs, and ova of *S. haematobium* have been found in these adhesions and in the free peritoneal fluid.

Schistosomiasis is hyperendemic in this region, being active or latent in almost all the population from the age of 5 years upwards. In the author's view this helminth causes widespread lesions in many parts of the body [see also GELFAND, this *Bulletin*, 1950, v. 47, 903] and may invade the walls of the stomach, giving rise to pyloric stenosis.

W. L. Harnett

CAMAIN, R. Aperçus sur le cancer en A.O.F. [**Survey of Cancer in French West Africa**] *Bull. Soc. Path. Exot.* 1954, v. 47, No. 4, 614–30. [25 refs.]

In this paper the author presents statistics of the malignant tumours examined at the Pasteur Institute at Dakar for the period 1942–53. There were 2,136 cases, of which 252 were in European and 1,884 in African patients.

Among the European patients epitheliomas were common, especially those to be expected in the 4th and 5th decades which are compatible with good general health, such as cancer of the breast and cervix uteri; internal

cancers causing deterioration in general health would have led to the repatriation of the patient. By reason of the comparative youth of the patients rodent ulcer and prostatic cancer were rare and sarcoma was relatively common.

Among Africans only a small proportion of the patients seen in hospital are followed up and reported as dead from the disease, 239 deaths among 1,849 seen in 1952 in a population of 17 million inhabitants of French West Africa; the remainder die at home and are not reported. From the author's figures it appears that epithelioma of the skin accounts for 13 per cent. of all cases, cancer of the liver for 26 per cent. and sarcoma of the haemopoietic organs for 13 per cent. The ratio of sarcoma to carcinoma is 1:4, whereas in Europe it is about 1:30. The explanation of this high rate is not to be found in any racial factors, for among West Indian and American Negroes the index is much the same as among whites; nor is it due to the shorter span of life of the African, though it is possible that the more rapid growth of sarcoma forces the patients into hospital sooner. The most likely factor, however, is the repeated assaults by trauma, parasites and viruses on the connective tissues which are thus stimulated to proliferation.

Two-thirds of the epitheliomas develop in phagedaenic [tropical] ulcers of the lower limbs, the cancerous change appearing 2–4 years from the start of the ulcer, though it may be delayed for 8–10 years, the age of the patient being immaterial; early metastases in the inguinal lymph nodes are frequent. Epithelioma of the penis forms only 2 per cent. of all cancers, owing to the practice of circumcision among the Mussulmans and other sects, and contrasts with its great frequency in Indo-China. Basal-cell carcinoma is found in 9 per cent. of patients but in only a few are the tumours found on the face. Cancers of the mouth, due to repeated traumata from tooth sticks, roots of teeth, etc., are 10 times as common as cancer of the tongue. Cancer of the cervix uteri is generally in the late stages when first seen. Although 70–80 per cent. of Africans are infected by *Schistosoma haematobium*, the parasite is found in only two-thirds of the patients suffering from carcinoma of the bladder.

Carcinoma of the gastro-intestinal tract accounts for only 5 per cent. of all malignant tumours, although duodenal ulcer and chronic inflammatory lesions are common; lung cancer is very rare. Primary cancer of the liver is by far the commonest form of cancer in Africans; four times as many males as females are affected, at all ages with the maximum incidence at 35 years. The hepato-cellular type is found in 97 per cent. of patients, the cholangio-cellular in 3 per cent.; in almost all cases there is preceding cirrhosis and the disease is fatal in a few months, from pulmonary metastases. Mammary cancer, like uterine cancer, is seen late; salivary cancers, most frequent in the parotid gland, are common, while prostatic cancer is much rarer than in Europe. Kaposi's angio-sarcoma, a condition said to form 17 per cent. of sarcomas in French Equatorial Africa, formed only 1 per cent. of sarcomas here. *W. L. Harnett*

Faure, L., Geyer, A. & Gueffier, G. Considérations sur l'éosinophilie tropicale. [**Observations on Tropical Eosinophilia**] *J. Méd. de Bordeaux.* 1954, Oct., v. 131, No. 10, 1199–206.

Three patients apparently suffering from tropical eosinophilia were observed in Indo-China. In each case the eosinophils were increased, counts varying between 59 per cent. and 90 per cent. All had an adenopathy of inguinal or axillary glands and in 2 cases a purulent discharge

was obtained on incising enlarged glands. Two patients showed hepato- and spleno-megaly. All 3 had pulmonary symptoms, which were severe in two cases, one patient suffering from bronchial spasm and the other from frank asthma. One suffered intense pruritus. All 3 complained of fatigue disproportionate to their physical condition and in one an anxiety state required psychological treatment.

An attempt to find microfilariae in diurnal and nocturnal blood was negative on each occasion, and parasites were not found on examination of lymph from excised glands. The histological structure of the glands, however, was characteristic of a filarial infection. This may take 3 forms:— in the acute stage a dense eosinophilic infiltration, in the subacute stage a disorganization of the follicular structure with nodules composed of multinuclear giant cells, followed by fibrosis in the chronic stage. It is unusual to find microfilariae in the subacute or chronic stages and this may account for the authors' failure to find them. Eosinopenia followed the administration of cortisone, a sign which is claimed to distinguish tropical eosinophilia from a simple eosinophilia following a parasitic infection [this *Bulletin*, 1954, v. 51, 512].

All 3 patients gave positive intradermal reactions to filarial antigens. Two were treated with Notézine [diethylcarbamazine], 0·4 gm. daily for 10 days, the first receiving 2 and the second 4 courses of treatment. In both the previously positive intradermal reactions were reversed. It was considered that in at least 2 of the patients the condition was of filarial origin: the question of the aetiology of tropical eosinophilia in general is discussed. *H. T. H. Wilson*

Chaudhuri, R. N., Aikat, B. K. & Sanjivi, K. S. **Tropical Eosinophilia.** *Indian J. Med. Res.* 1954, Oct., v. 42, No. 4, 635–60. [Numerous refs.]

PARASITOLOGY: GENERAL

Shrivastav, J. B. **Comparative Efficiency of Three Different Techniques for the Diagnosis of Cystic Forms of Intestinal Protozoa and Helminthic Ova in Faeces.** *Indian J. Med. Res.* 1954, Oct., v. 42, No. 4, 497–508.

On routine examination of faeces for protozoal and helminthic infections it was found that simple microscopy often revealed the presence of these when the concentration methods in use failed to do so. Accordingly studies were undertaken into the efficiency of the de Rivas acid-ether concentration technique [this *Bulletin*, 1928, v. 25, 447] and that of Faust [*ibid.*, 1940, v. 37, 62], which is a zinc sulphate centrifugal flotation method. Details of the performance of the tests and of the results achieved by them in the detection of common protozoa and helminths when applied to 100 specimens are set out at length in the text. The conclusion is reached that simple microscopy is of the greatest value in stool examination and that it cannot be replaced by either of the concentration methods mentioned; of the two latter the zinc sulphate flotation method is the more efficient, and it supplements the simple examination though it does not replace it.

A. R. D. Adams

Stauber, L. A. **Parasitological Reviews. Application of Electrophoretic Techniques in the Field of Parasitic Diseases.** *Exper. Parasit.* New York. 1954, Nov., v. 3, No. 6, 544–68. [Numerous refs.]

ENTOMOLOGY AND INSECTICIDES: GENERAL ZOOLOGY

McKiel, J. A., West, A. S. & Reed, G. B. **The Failure of the Antihistamine Cream Pyribenzamine to alleviate Reactions from Bites of the Mosquito** *Aedes aegypti.* *Mosquito News.* 1954, Dec., v. 14, No. 4, 196–9. [12 refs.]

" . . . tables show that two per cent pyribenzamine cream has exerted no significant effect on reactions to bites of the mosquito, *A. aegypti.* The disagreement between these results and those published by O'Rourke and Murnaghan can possibly be attributed to differences in technique which have already been discussed. In our test which followed O'Rourke and Murnaghan's method of applying creams after the bites were received, it was frequently noted that massage of either cream decreased or eliminated pruritus. It therefore appears that the massage of a cream is more important in relieving pruritus from mosquito bites than the presence of pyribenzamine in the cream."

See also p. 336, Portman, **Control of Mosquitoes in California Rice Fields.**

van Wymeersch, H. & Wanson, M. La porocéphalose nymphale et son image radiologique. [*Armillifer armillatus* **Infection and Its X-Ray Manifestations**] *Ann. Soc. Belge de Méd. Trop.* 1954, Aug. 31, v. 34, No. 4, 517–22, 2 figs. on 2 pls. [12 refs.]

Three cases of larval infestation of *Armillifer armillatus* in the Belgian Congo are reported. Diagnosis was on radiological evidence which is reproduced in two good photographs. No clinical condition was attributable to infection with the parasites, which were localized to the pulmonary region, the pelvis and abdominal cavity. The 3 cases were revealed in a series of 70,000 persons radiologically examined in the past few years. The paper discusses the differential diagnosis, on radiological appearance, of this type of infection from the cysticercus infection of the tapeworm, *Taenia solium.*

D. S. Bertram

Schoof, H. F. & Siverly, R. E. **Multiple Release Studies on the Dispersion of** *Musca domestica* **at Phoenix, Arizona.** *J. Econom. Entom.* 1954, Oct., v. 47, No. 5, 830–38, 3 figs.

A large-scale experiment, described in some detail, was carried out to observe the dispersion of *Musca domestica* from 5 sites, each of which was a natural source of large numbers of house-flies. About 70,000 flies were collected at each site and allowed to feed on radio-active milk (^{32}P) for 24 hours. They were then dusted or sprayed with a coloured dye, one colour to each of the sites. The sites were on the perimeter of Phoenix City. Collecting stations were established and the catches tested for radioactivity by Geigy counter. Positive individuals were then tested for dye in the usual way. About 6,000 tagged flies were recovered out of 342,000 released and the total catch of flies taken to obtain these tagged recoveries

was about 3½ million. It is concluded that although house-flies can disperse for 5 to 20 miles, the mass of a population is generally restricted to within ½ to 2 miles of its centre of origin; there is a good deal of random, meandering movement within these limits. One mile is recommended as the distance for fly control outside most communities [for previous studies by the authors, see this *Bulletin*, 1953, v. 50, 257]. *D. S. Bertram*

Lewis, C. T. **Studies concerning the Uptake of Contact Insecticides. I.—The Anatomy of the Tarsi of certain Diptera of Medical Importance.** *Bull. Entom. Res.* 1954, Dec., v. 45, Pt. 4, 711–22, 5 figs. [17 refs.]

The tarsi of the blowfly *Phormia terraenovae* and the tsetse fly *Glossina palpalis* are described and figured in some detail; in addition, those of *Musca domestica* were studied and some earlier descriptions corrected in certain details. The structure of the intersegmental joints and of the pulvilli is also considered. Any of these regions may be of importance (1) in the accumulation of small particles of insecticide, and (2) in the penetration and local toxicity of the insecticide.

Projections from the tarsi comprise: primary and secondary spines, bristles, chemoreceptors and microtrichia. The primary spines are mainly for propulsion and are best developed on the 2nd and 3rd pairs of legs, which provide the main forward thrust. Secondary spines and bristles are probably for protection of the delicate chemoreceptors. The last-named are special hollow setae, with a very thin frontal membrane of cuticle, apparently covered by a lipoid layer, through which lipoid-soluble insecticide might readily penetrate to the sensory neurocytes below. Counts of the chemoreceptors on all 6 legs showed that over 1,000 were present in *Musca* and *Phormia* and over 400 in *Glossina* (though tsetse flies have not been proved to possess a tarsal gustatory sense).

Experiments on the contamination of blowflies exposed to particulate deposits showed that the hind tarsi collected more fragments than the others. Particles adhere to the ventral spines and chemoreceptors and work their way down to their bases; however, the microtrichia prevent particles of over 10 μ reaching the general cuticle surface. The first tarsal segments on each leg, being most hairy, pick up more than the other segments or the pulvilli.

In regard to penetration of an insecticide, such as DDT, it is known that doses applied to different parts of an insect vary greatly in effect. One suggested route is via the thin-walled chemoreceptors.

However, Fisher [this *Bulletin*, 1953, v. 50, 69] found a gradient of increasing effectiveness as the point of application of DDT moved proximally up the leg of a fly; and this is not strictly correlated with the density of chemoreceptors. The author considers that the important factor is the number of sensory nerve fibres adjacent to the site of contact.

The pulvilli of all species investigated possess neither nerves, sense cells nor gland cells and are apparently not important as sites for entry of DDT.

J. R. Busvine

Nash, Ruth. **Studies on the Synergistic Effect of Piperonyl Butoxide and Isobutylundecyleneamide on Pyrethrins and Allethrin.** *Ann. Applied Biol.* 1954, Dec., v. 41, No. 4, 652–63, 1 fig. [22 refs.]

This paper describes a laboratory investigation of the relative synergizing powers of piperonyl butoxide [PB] and isobutyl undecyleneamide (IN 930) when mixed in different ratios with natural pyrethrins or with allethrin.

Tests were made with two kinds of insect, by different methods. House-flies (*M. domestica*) were treated individually by a droplet application method; and bed bugs (*Cimex lectularius*) were exposed to residues on treated filter papers.

Both synergists were tested at varying ratios to the insecticides, ranging from 1:1 up to 20:1. The toxicities of the mixtures increased with the proportion of synergist used, but the relative synergism fell off somewhat at ratios above 5:1 with the IN 930. The PB was the more powerful synergist, increasing the potency of pyrethrins 5 times and allethrin 4 times to flies, and pyrethrins twice and allethrin 3 times to bugs; whereas IN 930 did not raise the potency of either insecticide more than twice for either insect.

The addition of PB to residual films of pyrethrins prolongs their effectiveness because of the synergism; but an experiment to investigate the effect of PB on the stability of pyrethrin films showed that this effect, if present, must be only slight. *J. R. Busvine*

McCauley, W. E. & Sun, Y. P. **Dieldrin.** *Soap.* New York. 1954, Dec., v. 30, No. 12, 171–3, 195, 199, 3 figs. [40 refs.]

A general review.

Winteringham, F. P. W., Bridges, Patricia M. & Hellyer, G. C. **Mode of Insecticidal Action studied with Labelled Systems. Phosphorylated Compounds in the Muscle of the Adult Housefly,** *Musca domestica*, L. *Biochem. J.* 1955, Jan., v. 59, No. 1, 13–21, 5 figs. [30 refs.]

Harrison, J. L., Audy, J. R. & Traub, R. **Further Tests of Repellants and Poisons against Leeches.** *Med. J. Malaya.* 1954, Sept., v. 9, No. 1, 61–71.

The authors have already reported on their tests against leeches during which they used clothing impregnated with the all-purpose repellent M-1960 (equal parts of *n*-butylacetanilide, 2-butyl, 2-ethyl-1,3-propanediol and benzyl benzoate) [this *Bulletin*, 1954, v. 51, 1204].

This present paper is an account of other tests made at the same time with protective socks, ointments and poisons. The tests are described in detail and the results are given in 11 tables. It is admitted that they do not form a well planned whole but it is suggested that they do serve as useful pointers.

Woollen socks impregnated with M-1960 were of little value against water leeches but were most promising against land leeches: it is suggested that cheap canvas shoes impregnated with repellent may be better.

Repellent liquids were made up into ointments with 10–15 per cent. of an inert substance, Santocel C, as a base.

They contained (a) dimethyl phthalate [DMP]: (b) ethyl *beta* phenyl hydracrylate, and (c) a mixture of DMP, Rutgers 612 [2-ethylhexanediol] and dimethyl carbate. These ointments were applied directly to the skin of the legs of the volunteers. Against water leeches the ointments were worthless. Against land leeches they were more promising, though they have to be renewed at intervals.

The insecticides lindane, aldrin and dieldrin were tried against land leeches and though there was some sign of a reduction in numbers 2 days after spraying, it was not sufficient to give any confidence in the use of these insecticides as a control measure. *H. S. Leeson*

MISCELLANEOUS PAPERS

THE CENTRAL AFRICAN JOURNAL OF MEDICINE

The first issue of this new journal is dated January 1955; it is to be published bi-monthly and the annual subscription is £2 2s. 0d.

The intention of its sponsors is that this journal will become the means by which records of diseases important in this wide area of Africa may appropriately be made public. The clinical and pathological material on which contributions may be based exists plentifully throughout Rhodesia and Nyasaland, and it is to be hoped that those who work in this fruitful field will support the new publication by contributing the first-hand accounts of their experience which are essential to a thriving journal.

The Bureau of Hygiene and Tropical Diseases welcomes the journal and wishes success to Dr. Gelfand and his colleagues who have launched it.

Charles Wilcocks

RIBEIRO, A. L. **Multiracial General Practice in Nairobi.** *Brit. Med. J.* 1954, Oct. 23, 979–81.

This is an interesting short account of some of the difficulties of private practice in Kenya, where patients may be Europeans, Asians or Africans, with cultural and educational backgrounds of extreme diversity, and living in conditions which range from those of prosperity to great poverty and overcrowding. In addition to economic factors, religious and other customs dictate the diet of the people and reflect the intensity of their belief in witchcraft, and dictate also the restrictions placed on women, which formidably interfere with their health. It is not easy to see how the ill-effects of the purdah system can be overcome, or how the distrust recently displayed by the Kikuyu of any attempt to inject drugs can be countered, or how the social customs which in some tribes lead to such heavy incidence of venereal diseases can be changed. No doubt education and the force of imitation will gradually effect the necessary changes, as is happening in Moslem countries outside Africa, but the process seems slow. This short paper illustrates the difficulties to be overcome. *Charles Wilcocks*

MINTON, R., MULLER, S. & COHEN, G. **Fifty Years of American Medicine on the Isthmus of Panama.** *Amer. J. Trop. Med. & Hyg.* 1954, Nov., v. 3, No. 6, 951–63.

BARNICOT, N. A. & LADELL, W. S. S. **Physiological Effects of ACTH in some West African Subjects.** *J. Trop. Med. & Hyg.* 1954, Aug. & Sept., v. 57, Nos. 8 & 9, 180–91; 210–20, 9 figs. [45 refs.]

The authors studied the effects of corticotrophin on 6 male Africans. They point out that owing to the prevalence of malnutrition and parasitic disorders in Africans it is difficult to regard these subjects as normal, and they therefore refer to them as "reasonably representative of the local Nigerian population". Each subject was examined on a dosage of 40 mgm. of corticotrophin per day and later on a dosage of 100 mgm. per day. Investigations were made for 2 days prior to injection, 2 days over the injection period, and for 2 days subsequent to injection. An interval of about 8 weeks elapsed between the two dosage régimes, during which the subjects rested. The corticotrophin was supplied as acthar (Armour Co.),

made up in water or saline, latterly in saline because the aqueous solution was found to be painful. Injections were given intramuscularly every 6 hours over 36 hours. Frequent eosinophil and total leucocyte counts were made from finger prick samples; venous blood was examined for plasma corticoids, specific gravity (haemoglobin and serum protein), creatinine, uric acid, urea, sodium and glucose. The urine over the 6-day period was collected as 6-hour samples and examined for specific gravity and volume, 17-ketosteroids, creatinine, uric acid, urea, sodium and potassium. Selected samples of faeces were weighed and examined. Body weight was measured every 6 hours, rectal temperature every 6 hours, and hourly for the first 12 hours on the day of the large dose and on the last day. Blood pressure and pulse response to tilting were taken daily. Three meals of African food were consumed daily. The techniques and results are described in considerable detail.

The total leucocyte count rose during administration of corticotrophin. A fall in eosinophils was observed in 2 of the 6 subjects and was more pronounced on the larger dose. Urinary uric acid excretion increased in all subjects. Most showed some sodium and water retention, and a transient potassium diuresis. There was some rise in plasma corticoid levels and in 17-ketosteroid output.

The authors point out that critical comparison with Europeans would require that the experiments should be carried out under identical conditions with the same batch of hormone. What responses were observed, however, appeared to be within the normal European range.

B. G. Maegraith

Deschiens, R., Poirier, M. & Levaditi, J. Sur la réductibilité des hyper-éosinophilies non parasitaires par la pipérazine. [**Reduction of Non-Parasitic Eosinophilia by Piperazine**] *Bull. Soc. Path. Exot.* 1954, v. 47, No. 4, 521–4.

An eosinophilia may be consistently produced in the guineapig by intramuscular injections of an extract of the pimento *Capricum annuum* [this *Bulletin*, 1954, v. 51, 512].

Piperazine and its derivatives, particularly diethylcarbamyl-1-methyl-4-piperazine [Notézine, diethylcarbamazine] are effective in reducing this eosinophilia. It would appear therefore that piperazine has a direct effect on the eosinophils in addition to its anthelmintic action. Stimulation of suprarenals by piperazine derivatives may account for the reduction in eosinophils. Experiments with 9 guineapigs are described.

H. T. H. Wilson

REPORTS AND SURVEYS

India. **Report of the Malaria Institute of India for the Years 1948–1950** [Jaswant Singh, Director]. pp. ii + 95, 2 graphs. 1954. Delhi: Manager of Publications. [Rs. 3; 5s.]

The central Malaria Institute has a distinguished history of nearly 30 years and serves the Federal Government of India as both adviser and agent. Its functions therefore include the assembly of data on which the Director advises the Government on policy; a major research programme;

teaching—mainly at a high level; the management of experimental programmes in any part of India, and specific executive responsibility for control in the areas administered directly by Central Government. The Institute has also widened its scope to include studies of filariasis and kala azar, for which purpose a new unit attached to the Institute was ultimately established.

The report covers the critical years 1948 to 1950 immediately after the establishment of Government in its new form and the partition of India. The programme of work includes a great deal of consultative and advisory activity, much of which was concerned with the emergencies of that difficult time. The results of research have been published, mostly but not exclusively in the *Indian Journal of Malariology*. Studies cover a very wide field with particular emphasis on pharmacological enquiry into antimalarials, but including a variety of subjects covering the transmission and human stages of the parasite, and considerable detailed evaluations of the properties and proper formulations of insecticides. The well-known advanced course in malariology was further extended in time to 12 weeks and was well attended, while the Institute is now recognized by Calcutta University for advanced academic studies. Experimental programmes were undertaken in a number of places presenting special peculiarities, and the services of 4 joint WHO/UNICEF demonstration teams were secured. The Institute has contributed to progress in other countries by assignment of specialist staff on several international missions. The routine executive activities cover the coal-fields of India, the provinces of Delhi, Coorg, Ajmer-Merwara, and a few vital central Government projects such as the Assam Railway link. Data are given of the methods used and results achieved in each of these areas. The filariasis project was established under Major N. G. S. Raghavan in Madras and has now a record of considerable survey and a starting research programme, several parts of which have been published.

The report shows the great vitality of a prominent Institute which has already played an outstanding part in the study of the epidemiology of malaria and is clearly destined to play a similar part in its widespread control.

G. Macdonald

Laurie, W. **Survey before Service. Observations on Relation between Agriculture, Parasite Load, and Nutrition on a Tropical African Island.** *Lancet.* 1954, Oct. 16, 801–2.

It has been said that in medicine more diagnoses are missed through failure to examine the patient thoroughly than through lack of knowledge, and the same may be true of communities. Col. Laurie insists on the importance of thorough survey before prescribing for the control of disease, and illustrates his point by reference to a survey conducted by his unit (the East African Medical Survey) in the island of Ukara, Lake Victoria, where the 17,000 inhabitants are crowded to the extent of 600 to the square mile, and are heavily loaded with parasites, and yet lead satisfying, hard-working lives of great happiness.

The survey included 20 per cent. of the population, and the examinations were thorough; the chief findings were as follows: about 1 person in 30 was blind in one eye, usually from measles or smallpox; cheilosis was common in the early 'teens; splenomegaly was present in 36 per cent.; hydrocele and elephantiasis were common. Of the parasites found (and only 0·6 per cent. of the people examined were free from infection) hookworms were present in 38 per cent., *Ascaris* in 36, *Schistosoma mansoni* in 36 and *Strongyloides stercoralis* in 15 per cent. *Entamoeba histolytica* was

found in only 6 per cent. and *S. haematobium* in only 2 per cent. Microfilaraemia (*W. bancrofti*) was very common, the incidence rising to 36·8 per cent. at ages over 40. In children half the blood films examined showed malaria parasites. Haemoglobin levels were rather low, and the Kahn reaction was positive in up to 15 per cent. of persons free from leprosy, malaria and other complicating conditions.

Enquiries indicated that 25 per cent. of the children die before the age of 5 and 30 per cent. before the age of 22, but the population is likely to double itself in 60 years. Of patients attending one of the dispensaries, 20 per cent. had abdominal symptoms or intestinal worms, 15 per cent. chest troubles, 15 per cent. fever (mostly children) and a smaller group enlarged spleen (again mostly children). Tropical ulcer was not common. It is realized that the dispensary patients did not represent the true incidence of disease, for only 5 of the 256 persons on the island known to have leprosy attended the dispensary.

The people of this island show some minor signs of vitamin deficiency and somewhat unsatisfactory haemoglobin levels, yet in spite of the conditions of overcrowding they cannot be said to be suffering to any significant degree from undernutrition, and the reason seems to be that " under the spur of that most potent of all stimuli—famine " they have evolved a system of agriculture unique for Africa. Cattle are kept for farming, not as a means of storing wealth, they are mainly hand-fed in the owners' huts but their semi-decomposed bedding is used for manure, the islanders practise rotation of crops and the growing of forage crops, and great care is taken to prevent soil erosion.

The points made by the author are that agricultural development may be far more valuable than schemes for eradicating or treating disease, that a parasite survey is not necessarily a good measure for estimating health, and that a satisfactory system of mixed farming with cattle may provide the answer to food shortage. [This is a stimulating paper.] *Charles Wilcocks*

BOOK REVIEWS

Mozley, Alan [D.Sc., Ph.D., F.R.S.E.]. **An Introduction to Molluscan Ecology. Distribution and Population Studies of Fresh-Water Molluscs.** pp. x + 71, 15 figs. 1954. London: H. K. Lewis & Co. Ltd., 136, Gower Street, W.C.1. [9s.]

This short book is one of a series by the author [for earlier reviews see this *Bulletin*, 1953, v. 50, 321; 1954, v. 51, 128], and is sub-titled " Distribution and Population Studies of Fresh-Water Molluscs ". The author's intention is to survey what is known of the ecology of molluscs for the benefit of those medical and other workers concerned with the control of diseases transmitted by snails. The material presented is arranged, somewhat arbitrarily, in 6 chapters, a conclusion and 4 appendices. The author begins by stating some principles of animal ecology with particular reference to the distribution of snails, and passes to a consideration of certain aspects of the physical and biological environment which can limit snail distribution. He then briefly describes the snail

populations of certain representative habitats with particular reference to Baker's classic work on Lake Oneida in the St. Lawrence basin (Baker, *Tech. Pub. N.Y. State Coll. Forestry, Syracuse Univ.*, 1916 and 1918, Nos. 4 and 9) and to his own collecting in Central and Sub-Arctic Canada, and in Lake Baikal in Siberia. He emphasizes the localized distribution of those snails which transmit bilharzia, but does not attempt the delimitation of those types of habitats he considers to be " dangerous localities ". Perhaps the most important point made in the book is a brief generalization on the importance to the bilharzia parasite of those few habitats where the appropriate snail hosts are abundant *and* the exchange turn-over of the parasite is, for reasons of human usage, high. The author states " . . . some degree of control could be attained by the treatment of a relatively small number of localities with molluscicides. . . . My own opinion is that of all widespread parasitic diseases in Africa, bilharzia will prove to be the one which can be controlled most easily and most economically ". A brief discussion of the possible biological control of snails is followed by a short survey of the economic considerations in bilharzia control with particular reference to recent work in Egypt.

Thirteen of the illustrations reproduce photographs of habitats in North America, Finland and Siberia, which have no direct bearing on work on snails transmitting bilharzia. In the appendices are included brief summary life histories of *Schistosoma* and *Fasciola*, an inconclusive note on the nomenclature of host-snails, some suggestions for ecological work, and a suggestion that the genetic effects of radiation on snails might be of value.

[To workers concerned with the snail-borne diseases, this book will probably be of less value than its predecessors in the series by the same author. It contains original observations and recommendations, but the discursive style and inconsistencies in references to authorities are avoidable, and serve only to increase the vagueness of the account. It is to be regretted that the author has not seen fit to present his undoubted knowledge of the subject more concisely and in some better-edited format than the present repetitive series.] *W. Russell Hunter*

Gray, Peter. [Ph.D., D.I.C., F.R.M.S.] **The Microtomist's Formulary and Guide.** pp. xiii + 794. numerous figs. 1954. London: Constable & Co., Ltd., 10–12, Orange Street, W.C.2. [65s.]

This tremendous work has been undertaken by the Head of the Department of Biological Sciences at the University of Pittsburgh. It is divided into 2 parts, " The Art of Making Microscope Slides " and " Methods and Formulas used in making Microscope Slides ". A useful introduction sets out the scope and arrangement of the book and notes on special features such as methods of citing references, names of dyes and reagents, quantities and measures and the like.

The first part contains 16 chapters, which include methods of mounting, preparation of smears, different techniques for section and for injection of tissues. Each chapter begins with an account of general principles, and is then followed by a detailed description of typical examples.

The second part contains no less than 3,500 specific formulae and methods and where necessary the techniques for using them. Each chapter is subdivided decimally according to a scheme which is explained in full, so that every formula or technique may be identified. Here again, general considerations are discussed and in many cases, specific uses are described. The subject matter includes preservatives, fixatives, stains of general and

special application, accessory staining formulae, metal stains, solvents and oils, mounting and embedding media and various formulae.

There are 11 pages indicating books and periodicals cited and an Index of no less than 114 pages.

The book has not been written specifically for medical workers, but they will find all the general principles and usual staining methods included and their application catered for amply.

The reviewer has noted very few misprints but one requiring correction in a future edition is the spelling of the name of Jaswant Singh in the index.

It is difficult to think of any essential which has been omitted from this extremely valuable guide to practical microtomy: and the biological laboratory that does not include it in its library will be the poorer for want of a reference book of unusually comprehensive scope.

In defining that scope, the author refers to the " art of making microscope slides from biological specimens ". Few laboratory workers who have suffered the frustrations of struggling with some of the more refractory techniques of microtomy will quarrel with his use of the word " art ".

H. J. O'D. Burke-Gaffney

Ink, Jose. **Enfermedades infecciosas y parasitarias.** [Infectious and Parasitic Diseases.] Vol. I. pp. xv + 883. Vol. II. pp. xii + 887–1485, numerous figs. 1953. Buenos Aires: Lopez & Etchegoyen, S.R.L., Junin 863.

It is convenient to have all up-to-date information on this very considerable subject condensed into a book of two volumes, and this has been accomplished by Professor Ink of Buenos Aires. It is on the whole a good clinical study.

The first volume deals with a variety of eruptive fevers—measles, scarlet fever, rubeola, dengue, varicella, vaccinia, variola, erysipelas, rickettsioses, leprosy, erythema nodosum and multiforme, anaphylaxis, toxic dermatoses—and *acute infectious diseases*—sepsis and streptococcal infections, endocarditis, puerperal fever, epidemic angina, brucellosis, tetanus, diphtheria, carbuncles, rheumatism, encephalitis, rabies, psittacosis, lymphogranuloma venereum, trachoma, infective hepatitis, and epidemic parotitis. In passing it is intriguing to learn that in the Spanish language lymphogranuloma is still known as Nicolas-Favre disease.

In the second volume the following subjects are discussed in this order: *water-borne diseases*—salmonellosis, the dysenteric syndrome, leptospiroses, cholera; *tropical infections*—plague, yellow fever, pinta, relapsing fevers, tularaemia, yaws, verruga peruana, rat-bite fever; *acute respiratory infections*—influenza, atypical pneumonia, other infective respiratory diseases, whooping cough; *parasitic diseases*—malaria, leishmaniasis, Chagas's disease, parasitoses, scabies, myiasis, trypanosomiasis; *poisonous stings and bites and bacterial intoxications*—poisonous insects, snakes and fishes, botulism; *other tropical diseases*—mycoses, pellagra, beriberi, miliaria and toxoplasmosis. With such an array and such a mass of subjects to digest thoroughly, it becomes invidious to single out any particular item, but the following observations may be made. The author has adopted the principle of giving an adequate account of each disease without pretence to original observations, or delving deeply into the literature. It almost seems as if he had digested standard text-books, but he has included, at the end of each chapter, a résumé of the text in similar language to that

which has gone before. Thus, malaria occupies some 60 pages and the synopsis 9, which rather suggests waste of valuable space. While some diseases are treated at great length and in some detail, others are treated briefly and it is a matter of some surprise that such extremely important diseases, as pellagra, kwashiorkor, beriberi, sprue, miliaria, toxoplasmosis and several obscure syndromes, are dismissed in 8 pages to what might be termed a " mixed bag ". There is also a bibliography—a " national " list occupying 3 pages and a foreign list occupying one. The coloured plates are reproduced quite well on the whole, though the colouring is in places rather bright. *Philip Manson-Bahr*

NOTICE

ROSS INSTITUTE OF TROPICAL HYGIENE

Lay Course in Tropical Hygiene
To be held from 11th to 15th July, 1955

This course deals with malaria and its control and other tropical diseases and problems. It is intended for such people as estate and mine managers and their assistants, missionaries and all those whose work in the tropics makes them responsible for the health and welfare of others. Senior men will find the course of particular value owing to the many developments and great advances in knowledge of these subjects which have taken place in recent years.

There is no fee for the course.

It would be appreciated if agencies and firms would inform their managers and assistants that this course is being organised and encourage and assist them to attend.

About 11th June further information on the detailed arrangements will be sent to those who have enrolled.

Further details may be obtained from:—L. G. PONSFORD, Esq., *Organising Secretary*, Ross Institute of Tropical Hygiene, London School of Hygiene and Tropical Medicine, Keppel Street (Gower Street), London, W.C.1.

Printed in Great Britain under the authority of HER MAJESTY'S STATIONERY OFFICE
by The Eastern Press, Ltd., London and Reading.

(1755) Wt. P3/432 3/55 E.P. Ltd. Gp. 566.

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BUREAU OF HYGIENE AND TROPICAL DISEASES,
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London, W.C.1

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